CLINICL MANEGMENT OF DIABETES MELLITUS

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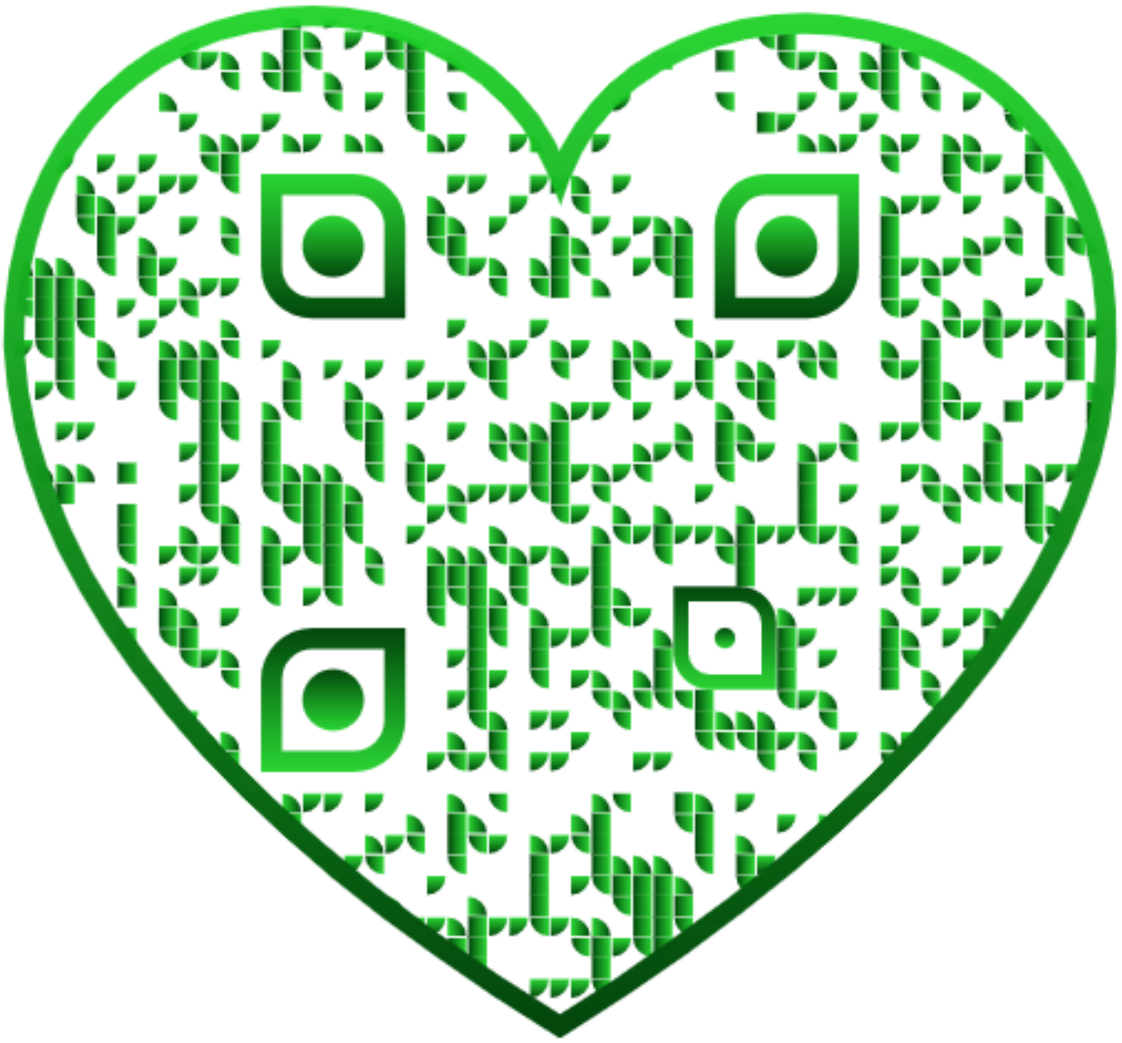

Course Topics:

1. Background and pathophysiology of diabetes
2. Diagnosis and classification of types of diabetes
3. Lifestyle and proper nutrition for diabetics
4. Technology used in diabetes management
5. Drug therapy for diabetes
6. Application of the American Diabetes Association (ADA) standards of care for diabetes patients for the year 2024
7. Continuous assessment of blood sugar and effectiveness of medications in diabetics.
8. Clinical management of complications of diabetes and gestational diabetes.

Section 1
Background and Pathophysiology of Diabetes

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BACKGROUND

- **Diabetes mellitus (DM) is a group of metabolic disorders characterized by chronically elevated blood glucose (BG) and abnormal carbohydrate, fat, and. protein metabolism**
- **It results from defects in insulin secretion, insulin sensitivity, or both.**
- **Without effective treatment, DM can lead to acute complications such as diabetic keto acidosis (DKA) and hyperosmolar hyperglycemic syndrome (HHS).**
- **Chronic hyper glycemia can cause microvascular, macrovascular, and neuropathic complications**

Regulation of Plasma Glucose Level

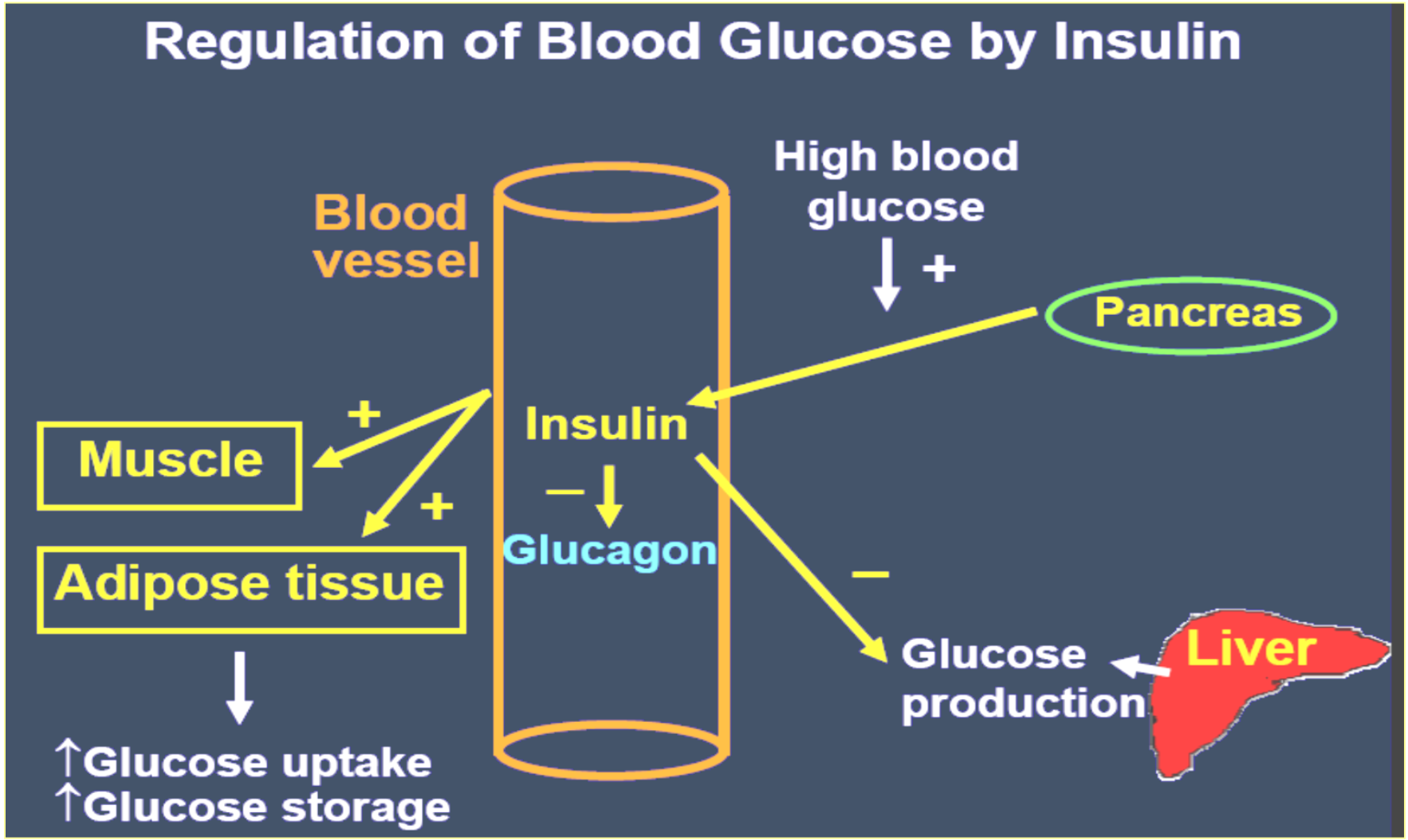
- Plasma glucose is tightly regulated by hormones:

Insulin: ↓ Plasma glucose

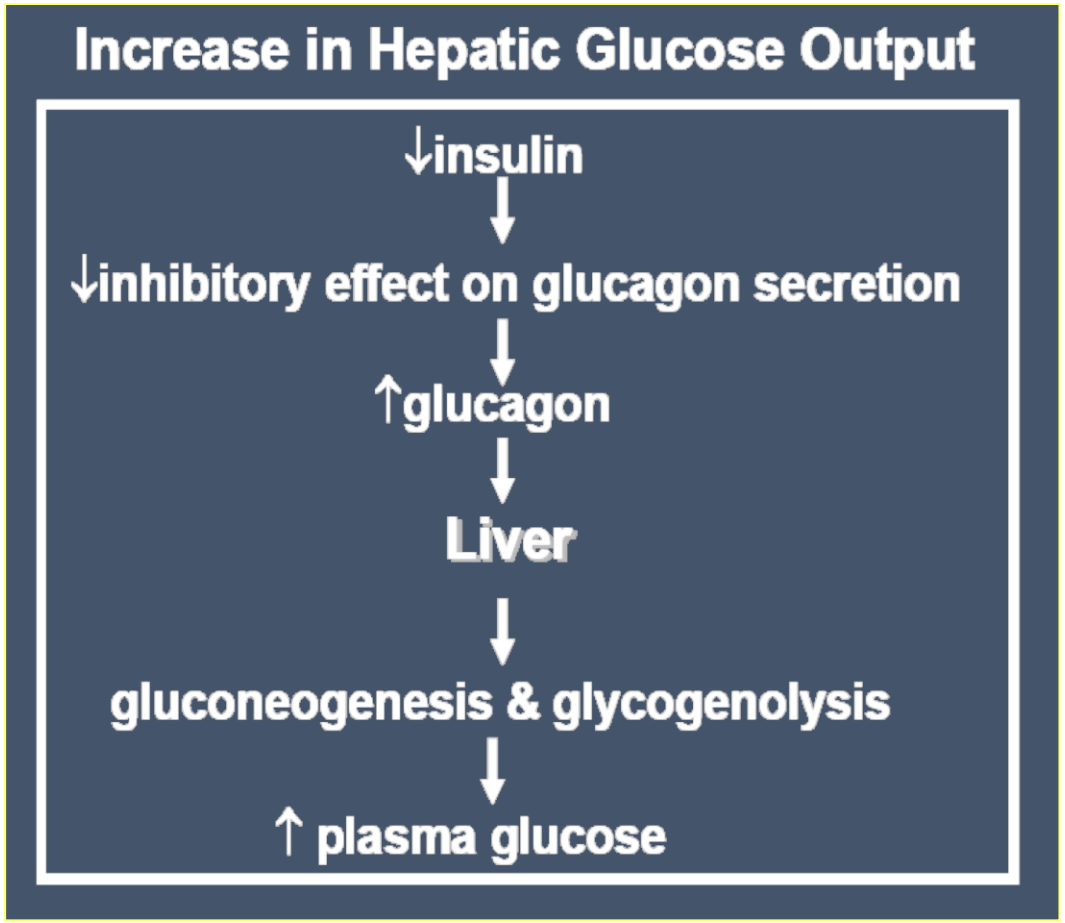
- Glucagon
  Epinephrine
  Cortisol
  Growth hormone

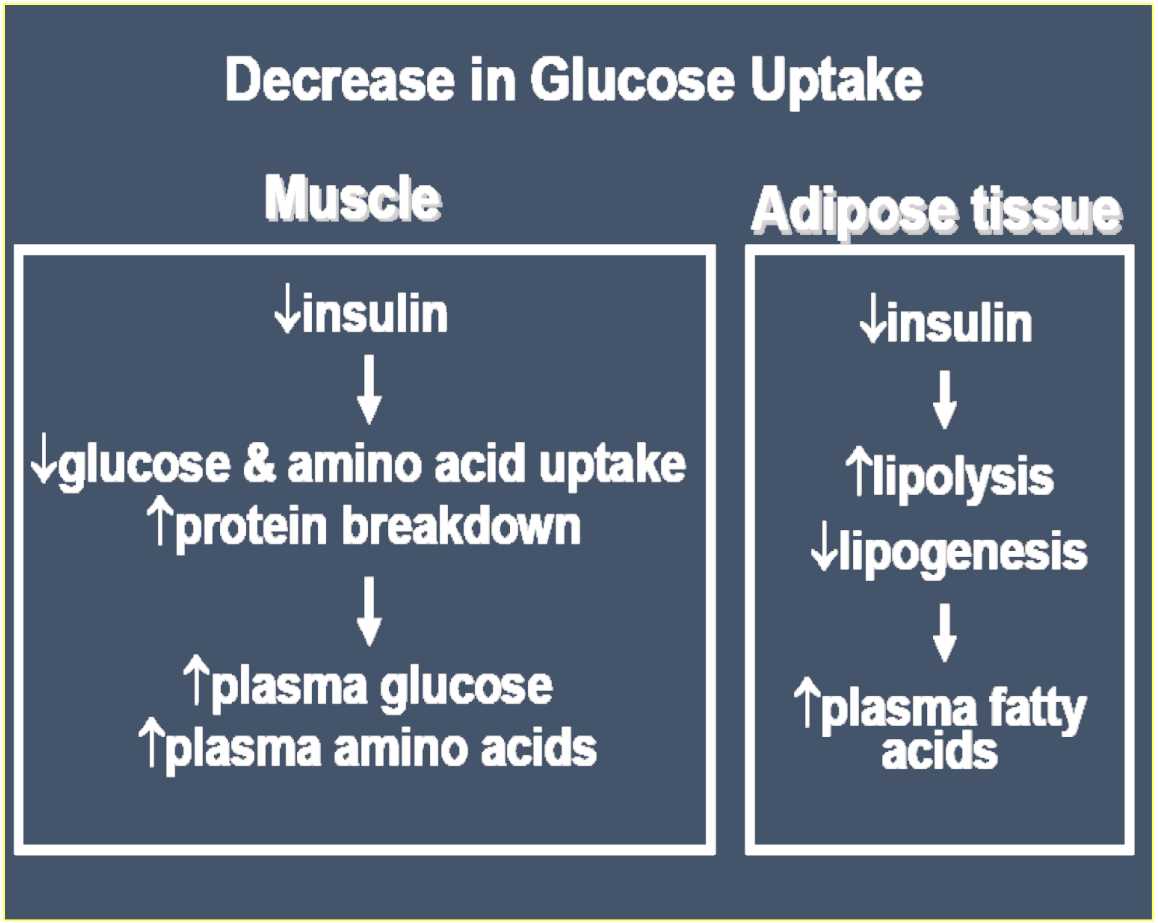
} ↑ Plasma glucose

How Insulin Decrease Plasma Glucose Level?

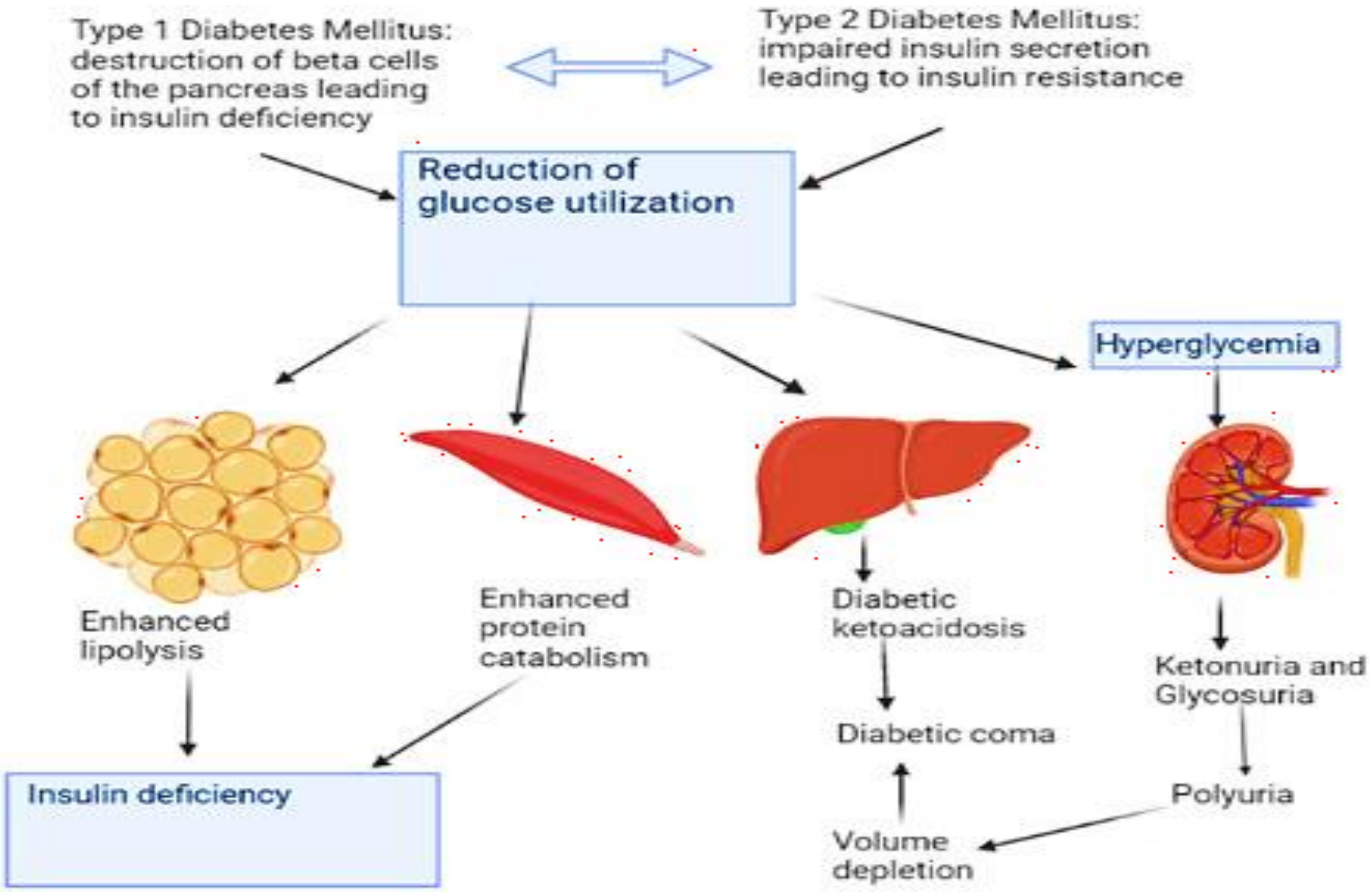


Pathophysiology of Diabetes Mellitus





Pathophysiology of Diabetes Mellitus


Type 1 Diabetes Mellitus: destruction of beta cells of the pancreas leading to insulin deficiency
Type 2 Diabetes Mellitus: impaired insulin secretion leading to insulin resistance
Reduction of glucose utilization
Hyperglycemia
Enhanced lipolysis
Enhanced protein catabolism
Diabetic ketoacidosis
Ketonuria and Glycosuria
Diabetic coma
Polyuria
Volume depletion
Insulin deficiency

Section 2
Diagnosis and Classification of Diabetes

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Diagnostic Tests for Diabetes

Additional Screening Guidelines

Condition	Clinical Tips	Best Test
An altered relationship between A1C and glycemia	A mismatch between A1C and glycemia could be caused by some hemoglobin variants, pregnancy (second and third trimesters and the postpartum period), glucose-6-phosphate dehydrogenase deficiency, HIV, hemodialysis, recent blood loss or transfusion, anemia, or erythropoietin therapy. People with HIV should be screened for diabetes and prediabetes before and 3–6 months after starting or changing antiretroviral therapy, and annually if initial results are normal.	Fasting plasma glucose
Acute pancreatitis	Screen for diabetes 3-6 months after an episode of acute pancreatitis and annually thereafter.	Any standard test for diagnosing diabetes
Cystic fibrosis	Annual screening should begin by the age of 10 years in all people with cystic fibrosis not previously diagnosed with cystic fibrosis-related diabetes	Oral glucose tolerance test
Posttransplantation status	Screen for hyperglycemia after organ transplantation. Posttransplantation diabetes mellitus should be diagnosed when the individual is stable on immunosuppressive therapy and free of acute infections.	Oral glucose tolerance test
Possible monogenic diabetes	Suspect monogenic diabetes in people diagnosed with diabetes in the first 6 months of life and in children and young adults with atypical characteristics of type 1 or type 2 diabetes, who often have a family history of diabetes in successive generations (suggestive of an autosomal dominant pattern of inheritance).	Any standard test for diagnosing diabetes plus appropriate genetic testing
Therapy with certain medications	Consider screening people for prediabetes or diabetes if they are on certain medications known to increase diabetes risk, such as glucocorticoids, statins, thiazide diuretics, some HIV medications, and second-generation antipsychotic medications.	Any standard test for diagnosing diabetes

Classification

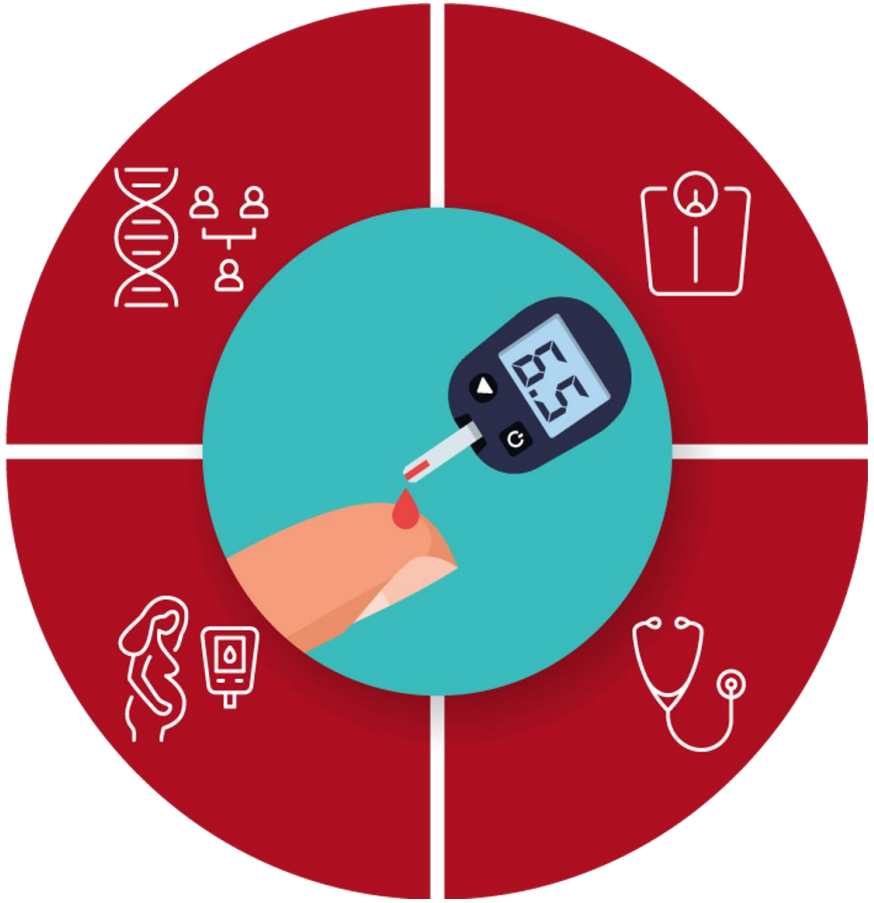
Classification of diabetes type is not always straightforward at presentation, and misdiagnosis is common.

Type 1 diabetes

(idiopathic or autoimmune β-cell destruction)

Gestational diabetes mellitus

(GDM; detected at 24–28 weeks of gestation in individuals without previously identified diabetes or high-risk glucose metabolism)



Type 2 diabetes

(non-autoimmune progressive loss of adequate β-cell insulin secretion frequently on the background of insulin resistance and metabolic syndrome)

Diabetes from other causes

(e.g., monogenic diabetes syndromes, diseases of the exocrine pancreas, and drug- or chemical-induced diabetes)

Screening Criteria for Prediabetes and Type 2 Diabetes

1) Informal assessment of risk factors

2) Validated risk calculator
FINDRISC Diabetes Risk Calculator

CLINICAL NOTES

- If results are normal, repeat screening at least every 3 years (annually for those with prediabetes), or sooner with symptoms or changes in risk.
- Risk-based screening for prediabetes or type 2 diabetes should be considered after the onset of puberty or after 10 years of age, whichever occurs earlier, in children and adolescents with overweight (BMI ≥85th percentile) or obesity (BMI ≥95th percentile) who have one or more risk factors for diabetes.

1) Informal Risk Factor Assessment for Prediabetes and Type-2 DM

Everyone ≥35 years of age

History of prediabetes

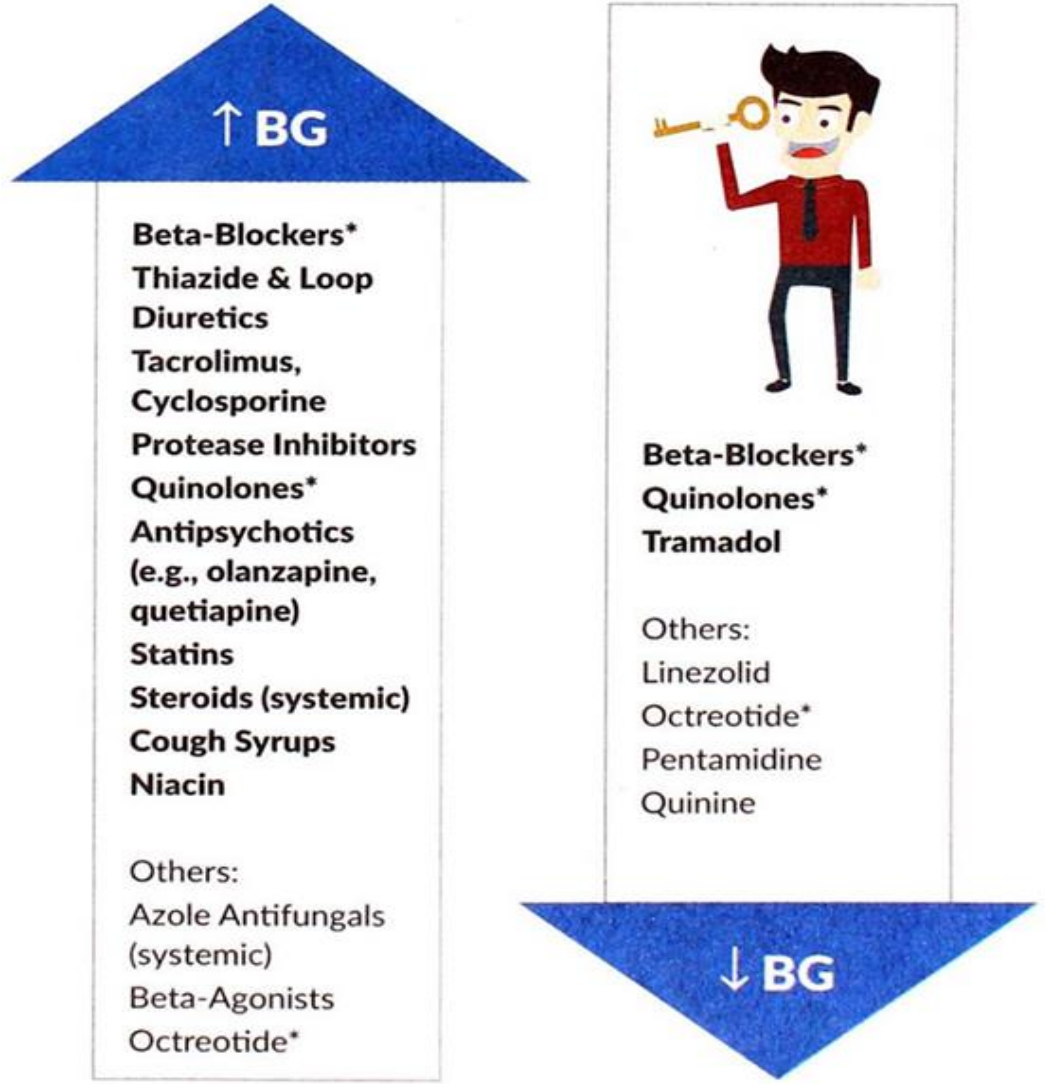
People with prior GDM

People with HIV, exposure to high-risk medicines, or a history of pancreatitis.

Adults (≥18 years of age) with overweight or obesity (BMI ≥25 kg/m^2 or ≥23 kg/m^2 in Asian American individuals) who have one or more of the following risk factors:

- First-degree relative with diabetes
- High-risk race/ethnicity
- History of cardiovascular disease
- Hypertension (≥130/80 mmHg or on therapy for hypertension)
- Polycystic ovary syndrome
- HDL cholesterol <35 mg/dL (<0.9 mmol/L) and/or triglycerides >250 mg/dL (>2.8 mmol/L)
- Physical inactivity
- Other clinical conditions associated with insulin resistance

➢ DRUGS THAT AFFECT BLOOD GLUCOSE



*Can cause hypo or hyperglycemia

2) Screening Criteria for Prediabetes and Type 2 Diabetes

FINDRISC Diabetes Risk Calculator

- INDRISC is a prediction tool to identify patients at risk of developing diabetes.
- It requires no laboratory testing and has been validated in multiple populations.
- FINDRISC uses age, BMI, physical activity, vegetable & fruit intake, medical treatment of hypertension, history of hyperglycemia and family history to determine risk of developing diabetes.
- By using FINDRISC to identify high-risk people and applying an educational intervention, it has been shown possible to reduce the incidence of diabetes.

https://reference.medscape.com/calculator/236/findrisc-diabetes-risk-calculator

- ✓ A risk score of **0-14 points** indicates a **low to moderate risk** of diabetes (1-17% chance of diabetes over 10 years).
- ✓ A risk score of **15-20 points** indicates a **high risk of diabetes** (33% chance of diabetes over 10 years).
- ✓ A risk score of **>20 points** indicates **a very high risk** of diabetes (50% chance of diabetes over 10 years).

Diabetes Types Comparison

Characteristics	Type 1	Type 2
% of diabetic population	5-10%	90%
Age of onset	Usually < 30 years + some adults	Usually > 40 + some obese children
Pancreatic function	Usually none	Insulin is low, normal or high
Pathogenesis	Autoimmune process	Defect in insulin secretion, tissue resistance to insulin, increased hepatic glucose output
Family history	Generally not strong	Strong
Obesity	Uncommon	Common
History of ketoacidosis	Often present	Rare except in stress
Clinical presentation	Moderate to severe symptoms: 3Ps, fatigue, weight loss, ketoacidosis	Mild symptoms: Polyuria and fatigue. Diagnosed on routine physical examination
Treatment	Insulin, Diet, Exercise	Diet, Exercise, Oral antidiabetics, Insulin

Which Type Is It?

What is recommended for diagnosing type 1 diabetes?
Misdiagnosis of type 1 diabetes is common and occurs in all age groups.

The AABBCC approach

A	**Age** (e.g., for individuals <35 years old, consider type 1 diabetes)
A	**Autoimmunity** (e.g., personal or family history of autoimmune disease or polyglandular autoimmune syndromes)
B	**Body habitus** (e.g., BMI <25 kg/m2)
B	**Background** (e.g., family history of type 1 diabetes)
C	**Control** (e.g., glucose management on noninsulin therapies)
C	**Comorbidities** (e.g., treatment with immune checkpoint inhibitors for cancer can cause acute autoimmune type 1 diabetes)

Staging of Type 1 Diabetes

	Stage 1	Stage 2	Stage 3
▪ Characteristics	▪ Autoimmunity ▪ Normoglycemia ▪ Presymptomatic	▪ Autoimmunity ▪ Dysglycemia ▪ Presymptomatic	▪ Autoimmunity ▪ Overt hyperglycemia ▪ Symptomatic
▪ Diagnostic criteria	▪ Multiple islet autoantibodies ▪ No IGT or IFG	▪ Islet autoantibodies (usually multiple) ▪ Dysglycemia: IFG and/or IGT ▪ FPG 100–125 mg/dl (5.6–6.9 mmol/L) ▪ 2-h PG 140–199 mg/dl (7.8–11.0 mmol/L) ▪ A1C 5.7–6.4% (39–47 mmol/mol) or ≥10% increase in A1C	▪ Autoantibodies may become absent ▪ Diabetes by standard criteria

Screening for type 1 diabetes?

1. Screen using autoantibodies
2. Monitor disease progression in individuals with preclinical type 1 diabetes.
    - Use the A1C test approximately every 6 months.
    - Conduct a 75-g oral glucose tolerance test annually, which includes fasting and 2-hour plasma glucose measures.
    - Adjust the frequency of monitoring based on an individual risk assessment.
    - Risk assessment should consider the individual's age, the number and type of autoantibodies present, and glycemic metrics.

Medication to delay the onset of type 1 diabetes

Teplizumab-mzwv infusion to delay the onset of symptomatic type 1 diabetes should be considered in selected individuals who are ≥8 years of age and have stage 2 type 1 diabetes.

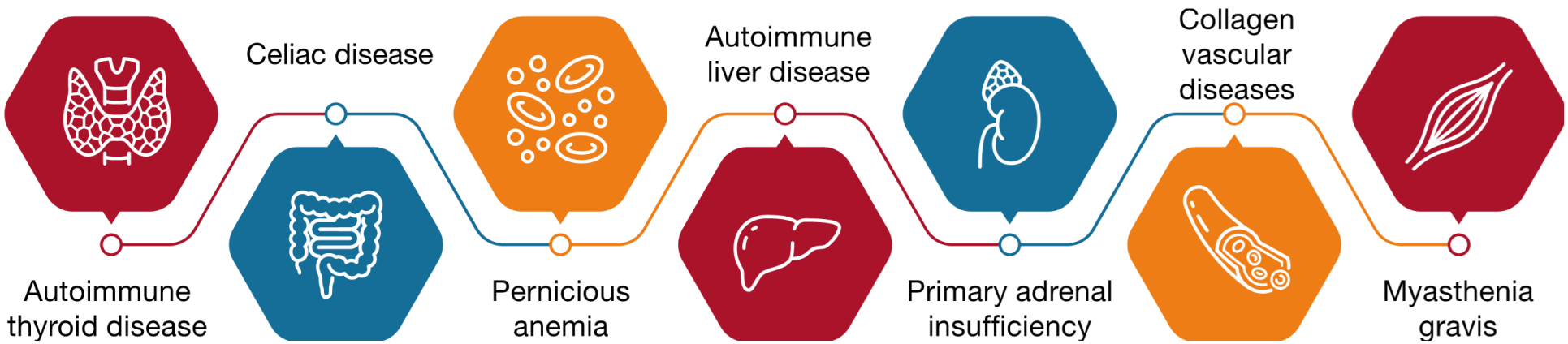
Assessment of Comorbidities

What autoimmune conditions should people with type 1 diabetes be screened for?

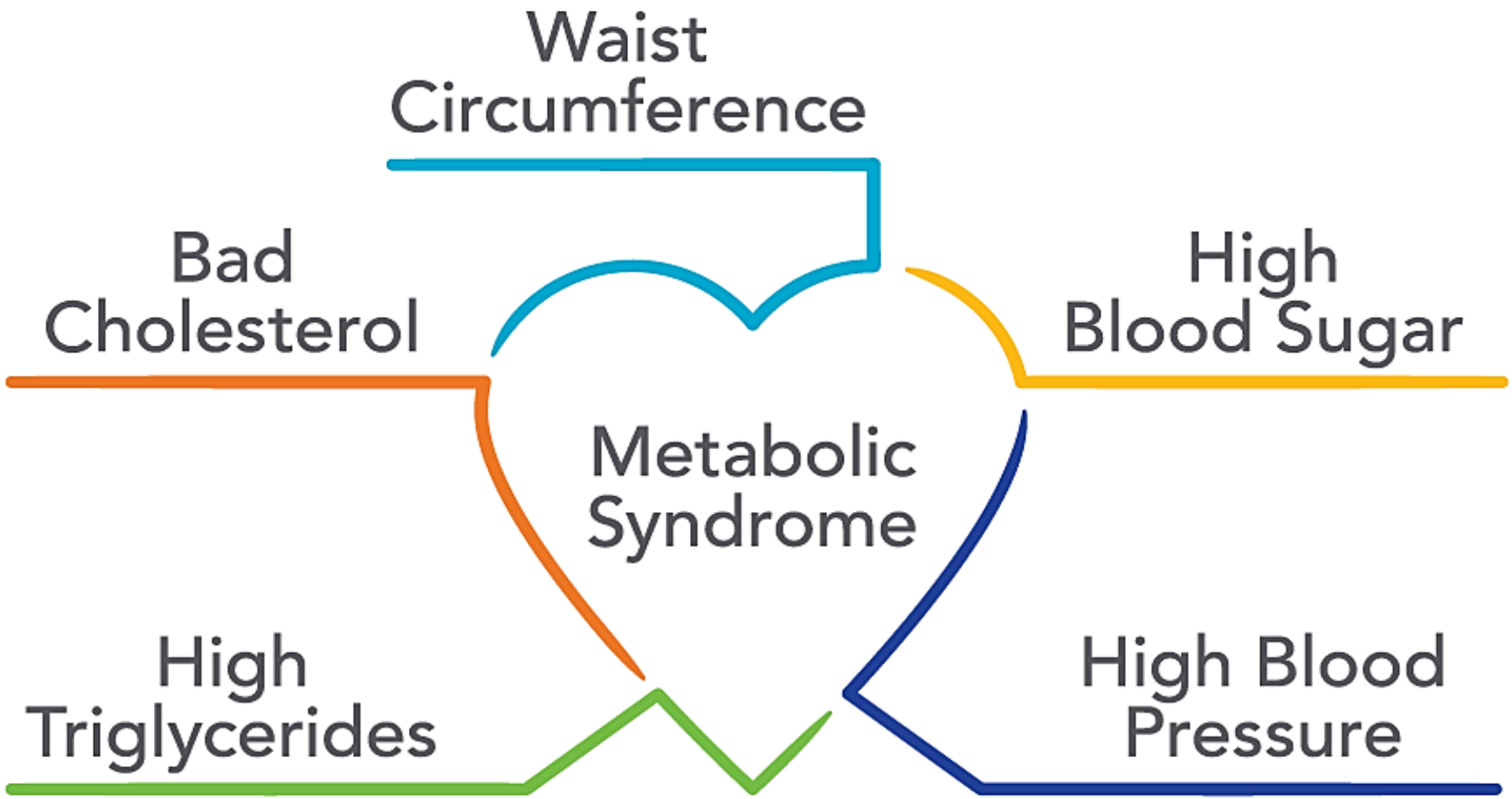
People with type 1 diabetes should be screened soon after diagnosis and periodically thereafter for:

- Autoimmune thyroid disease
- Other autoimmune conditions, if suggestive signs and symptoms are present

Autoimmune Conditions Associated With Type 1 Diabetes



Metabolic Syndrome and Diabetes



Section 3
Nonpharmacologic Therapy

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1- Management of Overweight and Obesity

A holistic approach to obesity management is essential, encompassing nutrition counseling, regular exercise, behavioral strategies, and diabetes self-management education to ensure effective and sustainable results.

Management of Overweight and Obesity

In people with type 2 diabetes and overweight or obesity, weight management should represent a primary goal of treatment along with glycemic management.

Weight management is crucially important because it:

- Delays progression from prediabetes to type 2 diabetes
- Is highly beneficial in treating type 2 diabetes
- Improves glycemia and reduces the need for glucose-lowering medications
- Reduces cardiovascular risk factors, lowering long-term cardiovascular and mortality risks
- Reduces other obesity-related health risks

When addressing weight management:

- Use person-centered, nonjudgmental, person-first language (e.g., “person with diabetes” rather than “diabetic person” and “person with obesity” rather than “obese person”).
- Calculate BMI and perform measures body fat distribution (e.g., waist circumference, waist-to-hip ratio, and/or waist-to-height ratio).
- Monitor obesity-related parameters at least annually to guide treatment decisions.

1- Management of Overweight and Obesity

Person-Centered Treatment Options for Overweight and Obesity in Type 2 Diabetes

	BMI (kg/m²)		
	25.0–26.9 (or 23.0–24.9*)	27.0–29.9 (or 25.0–27.4*)	≥30.0 (or ≥27.5*)
▪ Intensive behavioral counseling	✓	✓	✓
▪ Obesity pharmacotherapy		✓	✓
▪ Metabolic surgery			✓

*Recommended cut points for Asian American individuals.

1- Management of Overweight and Obesity

Nutrition, Physical Activity, and Behavioral Therapy for People With Overweight and Obesity

Recommendations
Nutrition, physical activity, and behavioral therapy to achieve and maintain ≥5% weight loss are recommended for people with type 2 diabetes and overweight or obesity.
Frequent counseling (≥16 sessions in 6 months) focusing on nutrition, exercise, and behavioral strategies to achieve a 500–750 kcal/day energy deficit, is beneficial for weight loss and recommended if available.
Long-term (≥1 year) weight maintenance programs are advised for those meeting weight loss goals, offering monthly support, weekly body weight monitoring, self-monitoring strategies, and regular physical activity (200–300 min/week).
Short-term, structured very-low-calorie diets (800–1,000 kcal/day) should be reserved for select individuals, prescribed by trained practitioners in medical settings with close monitoring, and include counseling for long-term weight maintenance.
When developing a plan of care, consider systemic, structural, and socioeconomic factors that may affect nutrition patterns and food choices, such as food insecurity and hunger, access to healthful food options, cultural circumstances, and other social determinants of health.

1- Management of Overweight and Obesity

Weight Loss Efficacy of Glucose-Lowering Medications

VERY HIGH	Semaglutide (injectable), tirzepatide
HIGH	Dulaglutide, liraglutide
INTERMEDIATE	Exenatide, lixisenatide, sodium–glucose cotransporter 2 inhibitors
NEUTRAL	Dipeptidyl peptidase 4 inhibitors, metformin

1- Management of Overweight and Obesity

Weight Loss Efficacy of Glucose-Lowering Medications

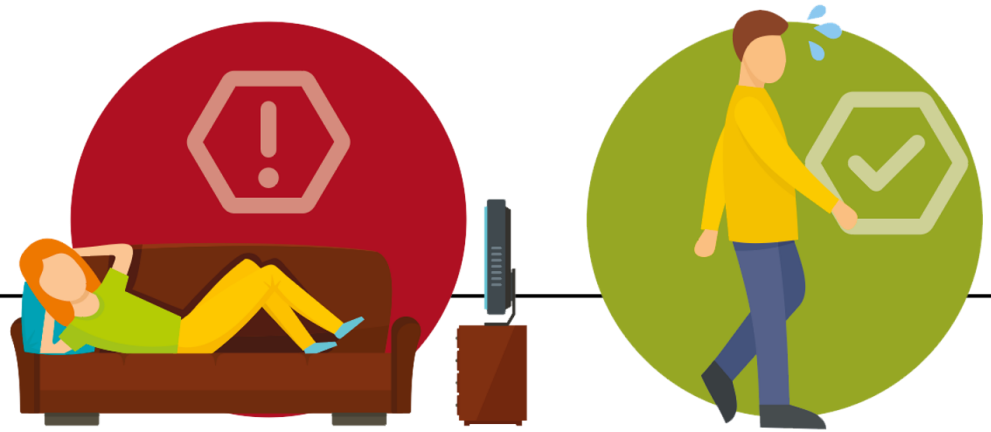
Glucose-Lowering Medications

- Consider weight when choosing glucose-lowering medications for individuals with type 2 diabetes and overweight or obesity.
- When possible, avoid prescribing medications that cause weight gain to treat comorbid conditions.
- Obesity pharmacotherapy should be considered for people with diabetes and overweight or obesity along with lifestyle changes. Potential benefits and risks must be considered.
- Continue obesity pharmacotherapy if it is effective (>5% weight loss after 3 months).
- Consider changing or stopping treatment if weight loss is <5% after 3 months or if significant safety/tolerability issues arise.

2- Diet and Physical Activity Recommendations for Adults at Risk for Type 2 Diabetes

Follow a Healthy Eating Pattern	Get Regular Physical Activity

▪ Emphasize whole grains, legumes, nuts, fruits, and vegetables and minimize refined and processed foods
▪ A variety of healthy eating patterns include:
  ▪ Mediterranean-style
  ▪ Low-carbohydrate
  ▪ Vegetarian or plant-based
  ▪ DASH (Dietary Approaches to Stop Hypertension)
	▪ ≥150 min/week of moderate-intensity physical activity, such as brisk walking
	▪ May include resistance or strength training
	▪ Break up prolonged sedentary time



2- Diet and Physical Activity Recommendations for Adults at Risk for Type 2 Diabetes

Key Nutrition Principles

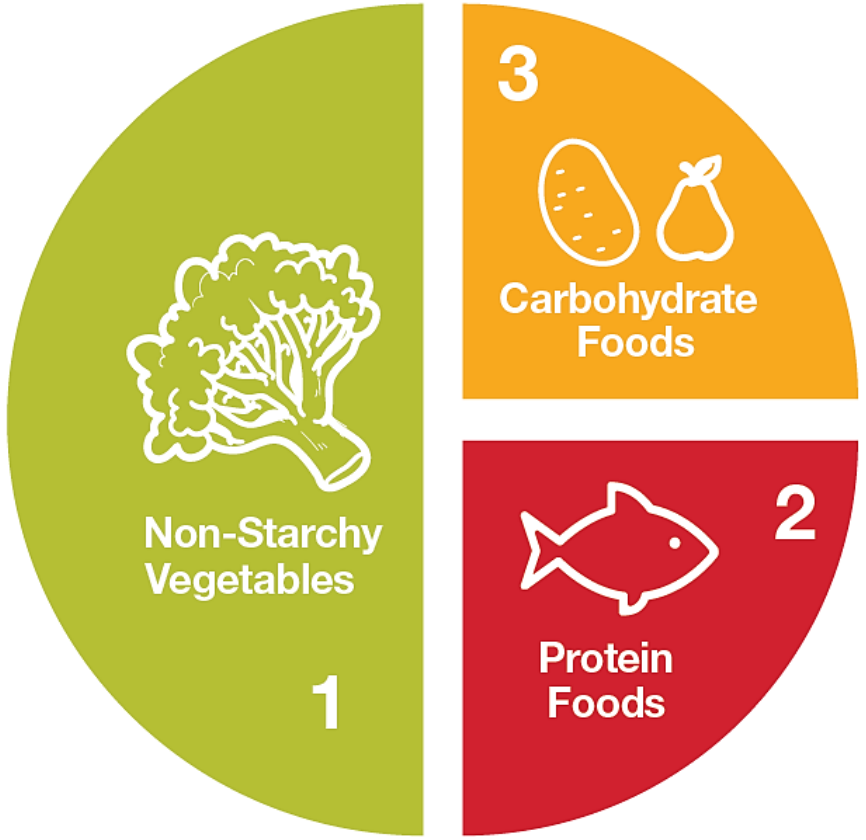
Data do not support a specific distribution of macronutrients. People with diabetes may choose from a variety of healthy eating patterns to fit their needs and preferences.

2- Diet and Physical Activity Recommendations for Adults at Risk for Type 2 Diabetes

❖ Nutrition for Life: Diabetes Plate Method

- **The Diabetes Plate Method is a helpful tool for anyone who wants to eat better and learn about variety and portion sizes, including people with prediabetes.**

- **Each section (based on a nine-inch plate) is for the following three food groups: vegetables, carbohydrates, and protein. These three food groups are the foundation for healthy eating.**



4- Medical of Nutrition Therapy MNT

There is a no one-size-fits-all eating pattern. Successful MNT programs are:

Flexible, realistic, and sustainable
Provided by a registered dietitian nutritionist
Offered to all people with type 1 or type 2 diabetes, prediabetes, and gestational diabetes mellitus
Screen for:
• Disordered eating
• Food insecurity
• History of dieting

5- Building positive health behaviors

Support positive health behavior through:	
Motivational interviewing	Problem-solving
Patient activation	Encouragement of health behavior self-monitoring, with or without clinician feedback
Goal-setting and action-planning	Identification of social support resources

5- Building positive health behaviors

Importance of 24-Hour Physical Behaviors for Type 2 Diabetes

	Glucose/ insulin	Blood pressure	A1C	Lipids	Physical function	Depression	Quality of life
SITTING/BREAKING UP PROLONGED SITTING	↓	↓	↓	↓	↑	↓	↑
STEPPING	↓	↓	↓	↓	↑	↓	↑
SWEATING (MODERATE-TO-VIGOROUS ACTIVITY)	↓	↓	↓	↓	↑	↓	↑
STRENGTHENING	↓	↓	↓	↓	↑	↓	↑
ADEQUATE SLEEP DURATION	↓	↓	↓	↓	?	↓	↑
GOOD SLEEP QUALITY	↓	↓	↓	↓	?	↓	↑
CHRONOTYPE/CONSISTENT TIMING	↓	?	↓	?	?	↓	?

Impact of physical behaviors on cardiometabolic health in people with type 2 diabetes

↑ Higher levels/improvement (physical function, quality of life); ↓ Lower levels/improvement (glucose/insulin, blood pressure, A1C, lipids, depression); ? no data available;
↑ Green arrows = strong evidence; ↑ Yellow arrows = medium strength evidence; ↑ Red arrows = limited evidence. Reprinted from Davies et al.

5- Building positive health behaviors

Building positive health behaviors and maintaining psychological well-being are foundational for achieving diabetes management goals and maximizing quality of life.

Essential tasks to help people with diabetes achieve their health goals:	
Refer for diabetes self-management education and support (DSMES)	Counsel on and support cessation of tobacco products and vaping
Refer for medical nutrition therapy (MNT)	Counsel on health behaviors
Counsel on routine physical activity	Support and refer to behavior health professionals for psychosocial care

6- Diabetes Self-Management Education and Support DSMES

DSMES Is Critical

People Who Benefit

- All people with diabetes

Advantages

- Ensures informed decision-making
- Promotes self-care behaviors
- Facilitates problem-solving
- Improved collaboration with the health care team
- Imparts knowledge and self-care skills
- Incorporates needs, goals, and life experiences

Times to Refer

- At diagnosis
- When not meeting treatment goals
- Annually
- When complicating factors develop
- When transitions in life and care occur

Appropriate Settings

- Group or individual visits
- In-person, telehealth, or digital platforms

Essential Components

- Provide culturally appropriate content
- Be responsive to individual preferences, needs, and values.
- Use positive, strength-based language that puts people first.
- Consider social determinants of health with a focus on health equity.

Proven Outcomes

- Improved diabetes knowledge, self-care, and quality of life
- Lower A1C and self-reported weight reductions
- Reduced all-cause mortality risk, acute care and hospital services utilization, and lower health care costs
- Increased use of primary care and preventive services
- Positive coping behaviors

7- Psychosocial Care for All People With Diabetes: Considerations and Recommendations

Screening

- ✓ Clinically significant mental health diagnoses are considerably more prevalent in people with diabetes than in those without.
- ✓ Clinicians should implement psychosocial screening protocols, including for diabetes distress.
- ✓ People with diabetes, caregivers, and family members should be screened at least annually or when changes in disease, treatment, or life circumstances occur.
- ✓ Address both clinical and subclinical psychological symptoms, which can affect the ability to carry out self-management, short-term glycemic stability, as well as mortality risk.

Resources are available to help health care professionals support behavioral and mental health in people with diabetes. Find them at https://professional.diabetes.org/meetings/behavioral-health-toolkit.

Diabetes Distress

The ongoing demands of diabetes self-care and the possibility or reality of disease progression are directly linked to reported diabetes distress.

High levels of distress:

- Significantly affect medication-taking behaviors
- Are linked to higher A1C, lower self-efficacy, and less-optimal eating and exercise behaviors

Section 4
Diabetes Technology

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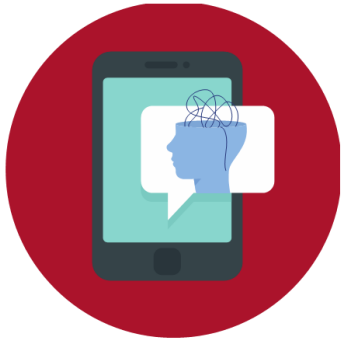
Diabetes technology includes:

Insulin pumps (also called continuous subcutaneous insulin infusion [CSII] systems) are insulin delivery devices that are worn on the body.

Connected insulin pens and pen caps are insulin delivery pens or related devices that can record and/or send insulin dose data and may also calculate doses.

Continuous glucose monitoring (CGM) systems and **glucose meters** are devices to monitoring glucose levels.

Automated insulin delivery (AID) systems connect a CGM system and an insulin pump with a control algorithm to deliver insulin automatically.



Diabetes self-management support software includes apps or online platforms that are intended to treat a medical or psychological condition or assist with data management or lifestyle modification.

General Diabetes Technology Principles

Assessment and medication selection
Diabetes devices should be offered to people with diabetes.
The type(s) and selection of devices should be individualized based on specific needs, preferences, and skill levels. For individuals, whose diabetes is partially or wholly managed by someone else (e.g., for young children or people with cognitive impairment or dexterity, psychosocial, and/or physical limitations), caregivers' preferences and skills should be taken into consideration.
When prescribing diabetes technology, provide people with diabetes and caregivers with ongoing education and support, in-person or remotely, on using the devices and managing/sharing the data they provide.
People with diabetes who have been using CGM, CSII, and/or AID for diabetes management should have continued access to these technologies across insurance payers, regardless their age or A1C level.
Starting CSII or AID early in the treatment of diabetes, even at the time of diagnosis, can be beneficial depending on individuals' or caregivers' needs and preferences.
Many diabetes-related digital apps and online platforms are available. These options vary widely in terms of quality and regulatory oversight. However, some people with diabetes or prediabetes may find such programs to be helpful sources of support, especially when combined with online coaching.

Blood Glucose Monitoring (BGM) Recommendations

BGM refers to fingerstick glucose checks done with a blood glucose meter. Encourage people who take insulin and use BGM to check their glucose when appropriate based on their insulin therapy. This may include:

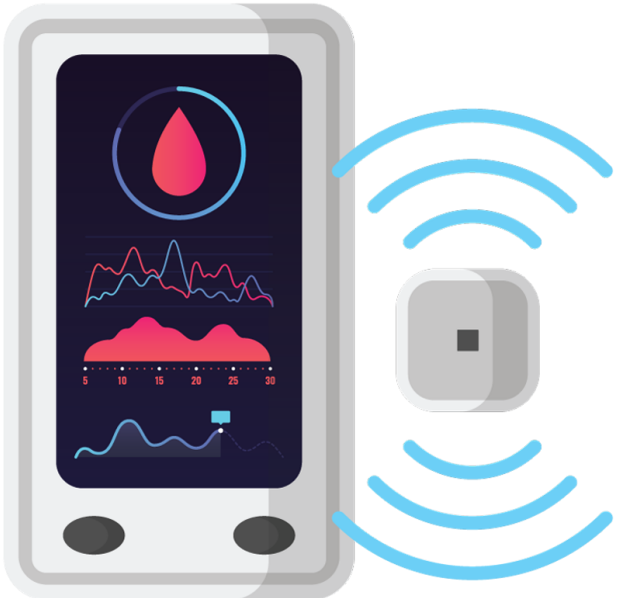
When fasting
Before meals and snacks
Occasionally after meals
At bedtime
In the middle of the night
Before, during, and after exercise
When hypoglycemia is suspected
After treating low blood glucose until normoglycemic
When hyperglycemia is suspected
Before and during critical tasks such as driving

BGM for noninsulin therapies:
May be helpful for adjusting meal plans, physical activity plans, and/or medications (particularly those that can cause hypoglycemia).

CGM Recommendations

There are different types of CGM systems, including:

- Real-time CGM systems, owned by individuals and measure and display glucose levels continuously.
- Intermittently scanned CGM systems, owned by individuals and measure glucose levels continuously but require scanning for visualization and storage of glucose values.
- Professional CGM systems, owned by clinics and intended to be used temporarily for 7–10 days to inform self-management and treatment decisions for people with diabetes. Data may be blinded or visible to the person wearing the device.



CGM Recommendations

Who can benefit from CGM?

- CGM should be offered for **adults with diabetes using insulin therapy** (basal only, multiple daily injections, or pump therapy).
- CGM should be offered for **youth with type 1 or type 2 diabetes using multiple daily injections or insulin pump therapy**.
- CGM can be helpful as an adjunct to BGM for **pregnant individuals with diabetes.**
- Periodic use of personal or professional CGM can be helpful for diabetes management **when consistent use is not desired or available.**

Section 4

Pharmacologic Therapy For Diabetes

By: Dr. Rezg Yousef Al-Sunah
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Diabetes Drugs:

A) Oral Medications:

1. Biguanides

Metformin (Glucophage)

2. Sulfonylureas

.Glipizide (Glucotrol,
Glyburide (DiaBeta)
Glimepiride (Amaryl)
Tolazamide (Tolinase)

3. Meglitinides

Nateglinide (Starlix)
Repaglinide (Prandin)

4.Thiazolidinediones TZDs

Pioglitazone (Actos)
Rosiglitazone (Avandia)

5. α-glucosidase Inhibitors

Acarbose (Precose)
Miglitol (Glyset)

6. DPP-4 Inhibitors

Sitagliptin (Januvia)
Saxagliptin (Onglyza)
Linagliptin (Tradjenta)
Alogliptin (Nesina)

7. SGLT2 Inhibitors

Canagliflozin (Invokana)
Dapagliflozin (Farxiga)
Empagliflozin (Jardiance)

Diabetes Drugs:

B) Injectable Medications

1. Insulin

- Rapid-acting: Lispro (Humalog), Aspart (NovoLog), Glulisine (Apidra)
- Short-acting: Regular insulin (Humulin R, Novolin R)
- Intermediate-acting: NPH insulin (Humulin N, Novolin N)
- Long-acting: Glargine (Lantus, Toujeo), Detemir (Levemir), Degludec (Tresiba)

2. GLP-1 Agonists

- Exenatide (Byetta, Bydureon)
- Liraglutide (Victoza)
- Dulaglutide (Trulicity)
- Semaglutide (Ozempic, Rybelsus)
- Lixisenatide (Adlyxin)

3. Amylin Agonists

- Pramlintide (Symlin)

1- Insulin

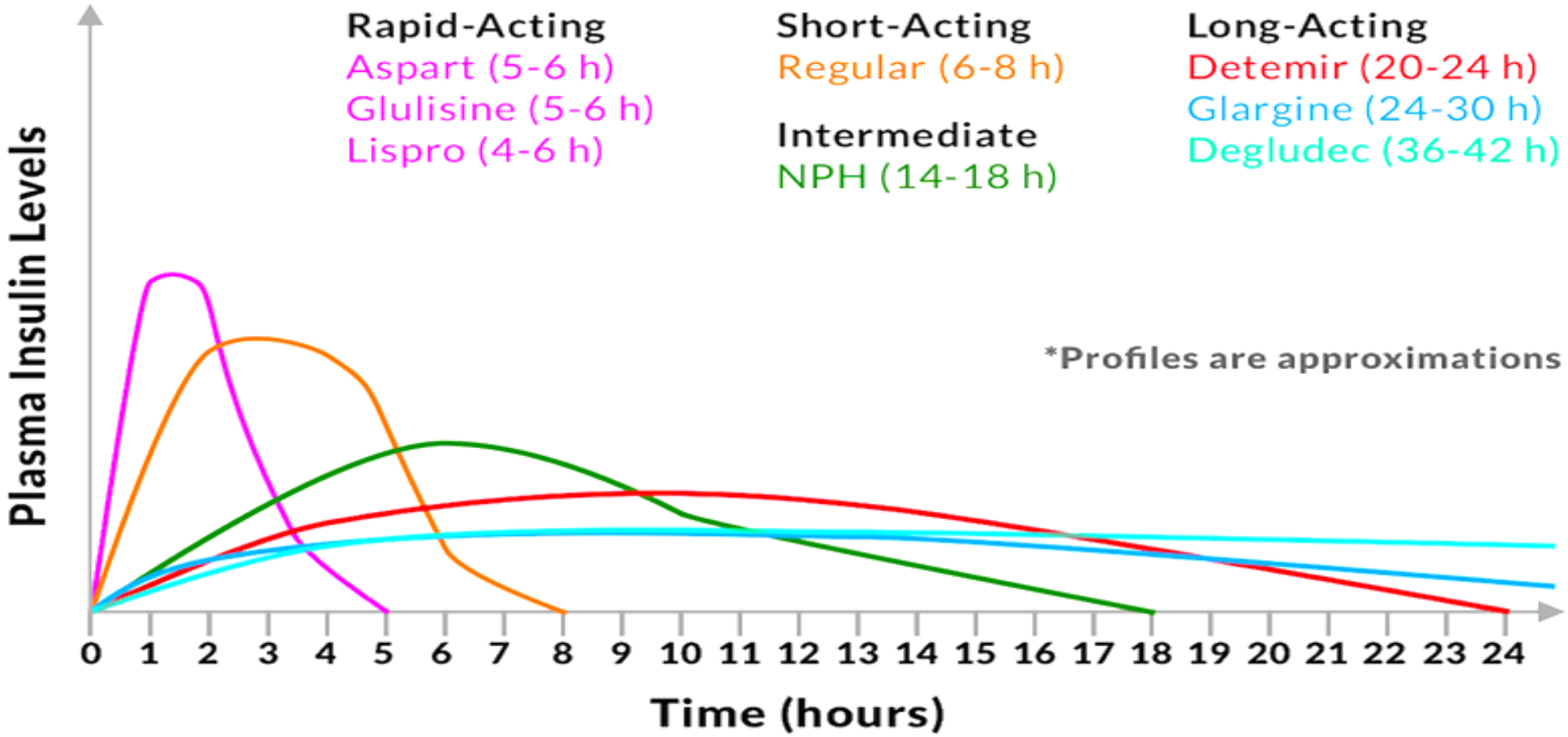
Efficacy:	**High to very high**
Doses:	**• Type 1 DM: 0.5 to 0.6 units/kg • Type 2 DM: 0.7 to 2.5 units/kg**
Hypoglycemia:	**Yes**
Weight change:	**Gain**
CV effects:	**Neutral**
Renal effects:	**Neutral**
Renal adjustment:	**Lower dose required**
Additional consideration:	**Inj. Site reaction**

Type of Insulin[a] by Generic (Brand) Name	Onset	Peak[b]	Duration[b]
Ultra-rapid acting			
Insulin aspart (Fiasp)	15–20 min[c]	90–120 min	5–7 hours
Insulin human—inhaled (Afrezza)	12 min	35–55 min	1.5–4.5 hours
Rapid-acting			
Insulin aspart (NovoLog)	10–20 min	30–90 min	3–5 hours
Insulin lispro U-100, U-200 (Humalog)			
Insulin glulisine (Apidra)			
Short-acting			
Regular (Humulin R, Novolin R)	30–60 min	2–4 hours	5–8 hours
Intermediate-acting			
NPH (Humulin N, Novolin N)	2–4 hours	4–10 hours	10–24 hours
Regular U-500 (Humulin R 500)	15 min	4–8 hours	13–24 hours
Long-acting			
Insulin detemir (Levemir)	1.5–4 hours	6–14 hours[d]	16–20 hours
Insulin glargine (Lantus, Basaglar)	2–4 hours	No peak	20–24 hours
Insulin glargine U-300 (Toujeo)	6 hours	No peak	36 hours
Insulin degludec U-100, U-200 (Tresiba)	1 hour	No peak	42 hours

Insulin

Type of Insulin[a] by Generic (Brand) Name	Onset	Peak[b]	Duration[b]
Combination Products			
70% NPH/30% Regular (Humulin 70/30, Novolin 70/30)	30–60 min	Dual	10–16 hours
75% NPL, 25% lispro (Humalog 75/25)	5–15 min		10–16 hours
50% NPL, 50% lispro (Humalog 50/50)	5–15 min		10–16 hours
70% insulin aspart protamine, 30% insulin aspart (NovoLog 70/30)	5–15 min		15–18 hours

Insulin Classes and Action Profiles



Basal insulin

- Refer to the longer-acting insulins that regulate BG levels in between meals by suppressing hepatic glucose production and maintaining near-normal glycemic levels in the fasting state

Bolus insulin

- Refers to short- or rapid-acting insulins that cover meals (also called prandial insulin) or glycemic excursions (also called correction insulin).

Premixed Insulin

- **70/30 MIXES**
  70% NPH/30% regular (Humulin 70/30, Novo/in 70/30)
  70% aspart protamine/30% aspart (Novolog Mix 70/30)
- **75/25 MIX**
  75% lispro protamine/25% lispro (Humatog Mix 75/25)
- **50/50 MIX**
  50% lispro protamine/50% lispro (Humatos Mix 50/50)

CASE SCENARIO

A 35-year-old female injects Humulin 70/30 60 units before breakfast and 20 units before dinner.

What is her TDD of regular insulin?

- **Humulin 70/30 Is 70% NPH and 30% regular.**
- **The regular dose in the morning is 60 units x 0.3 = 18 units.**
- **The regular dose In the evening is 20 units x 0.3 = 6 units.**
- **The TDD of regular insulin Is 24 units.**

Insulin Available OTC

- **Regular, NPH and premixed 70% NPH/30% Regular insulins can be sold OTC or can be dispensed with a prescription for insurance coverage.**
- **All basal and rapid-acting insulins are available by prescription only.**

Selecting an Insulin Syringe

- **Use the smallest syringe that will hold the units of insulin. It is easier to read the unit markings on smaller syringes, which makes them more accurate.**
  - **0.3 mL syringe for up to 30 units**
  - **0.5 mL syringe for 30 - 50 units**
  - **1 mL syringe for 51 - 100 units**

A 1 mL U-100 insulin syringe holds up to 100 units. Use smaller syringes to inject up to 50 units.

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DISPENSING INSULIN

- Dispensing insulin in an outpatient pharmacy requires a calculation of the days' supply and rounding up to the nearest vial/pen size.

- For example, if a patient is taking 35 units of Lontus daily, how many Lantus SoloStar pens would be dispensed to provide a 30-day supply?

Step 1: calculate the total number of units needed. 35 units/dayx30 days = 1,050 units of insulin needed

Step 2: calculate the number of units per insulin pen, based on the concentration of insulin.
Lantus 100 units/ntL x 3 mL per pen = 300 units per pen

Step 3: calculate the number of pens to be dispensed. Remember. 1 pens cannot be broken, so round up.
1,050 units needed x (1 pen / 300 units; = 3.5 pens

Answer 4 pens must be dispensed to provide enough Insulin

Remember: insulin pens require priming with 2 units prior to each dose. Some pharmacists account for this in their calculation of days' supply, but it is not a standard practice to do so.

Injection Areas

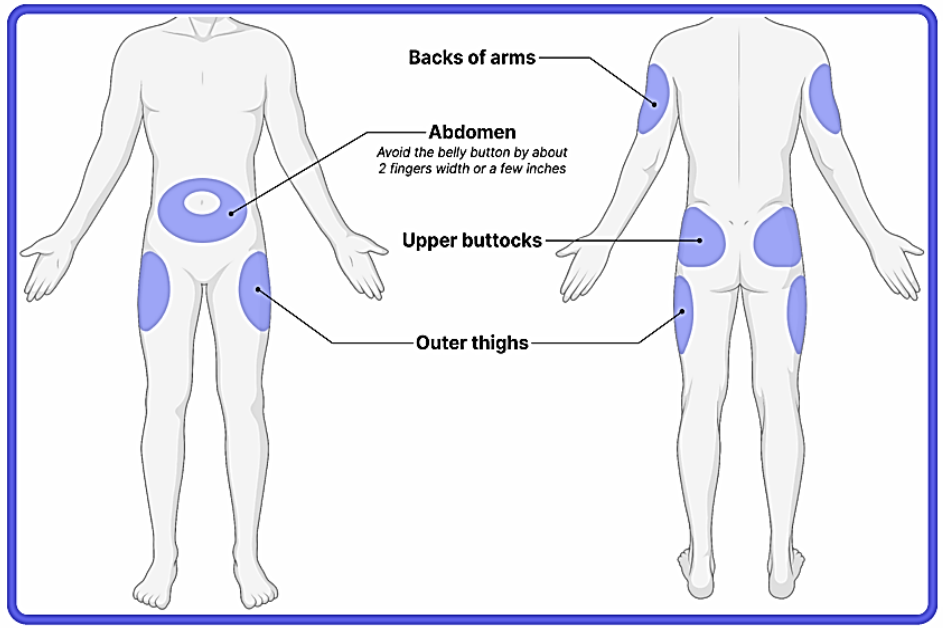
Insulin Injection Areas

Insulin is **best absorbed** when injected into the **abdomen** (staying away from the belly button by about 2 fingers width or a few inches); however, the outer thighs, upper buttocks and backs of arms are also acceptable injection areas.

Using the **same injection area** (e.g., abdomen) for each administration can help ensure the body receives **consistent levels** of insulin.

Rotate injection sites (in the same general body region) to prevent **skin damage**.

If using a **GLP-1 RA** or **GLP-1/GIP RA** with insulin, administer at **separate injection sites** and do **not** mix the medications. The injection sites may be in the same body region but should not be adjacent to each other.



2- glucagon-like peptide-1 (GLP-1)

Efficacy:	**High to very high**
Drugs Names:	**Dulaglutide, Exenatide, exenatide XR, Lixisenatide Liraglutide, and Semaglutide**
Hypoglycemia:	**No**
Weight change:	**Loss**
CV effects:	**Neutral HF, benefit MACE (some agents)**
Renal effects:	**Benefit (some agents)**
Renal adjustment:	**Exenatide, lixisenatide**
Additional consideration:	**Thyroid C-cell tumors**

MACE: Major adverse cardiovascular events

2- glucagon-like peptide-1 Receptors Agonist (GLP-1 RA)

- **Mechanism of Action:** **Synthetic analog of human GLP-1 that binds to GLP-1 receptors, resulting in glucose-dependent insulin secretion, reduction in glucagon secretion, and reduced gastric emptying; promotes satiety.**
- **The GLP1-RAs are administered SC**

- **Short-acting agents(exenatide, lixisenatide) : Predominantly lower postprandial glucose (PPG) levels**
- **Long-acting agents (dulaglutide, liraglutide, exenatide XR, semaglutide): Lower both FPG and PPG, but with larger effectson FPG**

- **The most common adverse effects:**
  Nausea, vomiting, diarrhea (dose related & dose titration), Injection site reactions and Hypersensitivity reaction

GLP-1 RAs and GLP-1/GIP RA: Efficacy and Safety

DRUG	RELATIVE A1C LOWERING*	CARDIORENAL EFFECTS	RELATIVE WEIGHT LOWERING*	RELATIVE GI SIDE EFFECTS
Dulaglutide *Trulicity* SUBQ injection	●●●●	**FDA approved for CVD benefit** **Evidence for renal benefit**	●●●	●●●
Exenatide *Byetta* SUBQ injection	●●	No data	●●	●
Exenatide ER *Bydureon BCise* SUBQ injection	●●	Neutral CVD effect	●●	●
Liraglutide^ *Victoza* SUBQ injection	●●	**FDA approved for CVD benefit** **Evidence for renal benefit**	●●●	●●
Semaglutide^ *Ozempic* SUBQ injection	●●●●	**FDA approved for CVD benefit** **Evidence for renal benefit**	●●●●	●●●
Semaglutide *Rybelsus* Oral tablet	●●●	Neutral CVD effect	●●●	●●
Tirzepatide** *Mounjaro* SUBQ injection	●●●●●	*Under investigation for CVD and renal benefit*	●●●●●	●●

2- glucagon-like peptide-1 Receptors Agonist (GLP-1 RA)

❖ Contraindications and precautions

i. **Impaired renal function: CrCl less than 30 mL/minute for either exenatide formulation; less specific for liraglutide. No dose adjustment necessary with semaglutide**
ii. **Caution with a history of severe GI tract disorder, particularly gastroparesis**
iii. **History of pancreatitis**
iv. **For liraglutide, semaglutide, dulaglutide, once-weekly exenatide: Contraindicated in patients with a personal or family history of medullary thyroid carcinoma (adverse effect found in rodent studies but not in humans)**

3- GLP-1/glucose-dependent insulinotropic polypeptide agonist

- ✓ **Mechanism of action**: **Similar to GLP-1 agonists above**
- ✓ **Tirzepatide: is the only agent currently approved for treatment of T2D**.
- ✓ **Dosing**
  - **i. Initial: 2.5 mg subcutaneously once weekly**
  - **ii. Increase at monthly intervals to 5, 10, or 15 mg once weekly**
- ✓ **Adverse effects:** Similar to GLP-1 agonists
- ✓ **Contraindications and precautions**: Similar to GLP-1 agonists
- ✓ **Efficacy**
  - **i. 2.0%–2.3% reduction in A1c, also decreases body weight**
  - **ii. Targets both fasting and postprandial glucose excursions**

4- Injectable Amylin Analogues (Pramlintide)

- **Mechanism of action**:
  i. Synthetic analog of amylin, a neurohormone co-secrete from the cells with insulin.
  Ii. Suppresses inappropriately high postprandial glucagon secretion, increases satiety, which may result in weight loss, and slows gastric emptying
- **A1C reduction ~ 0.6%**
- **Used as adjunctive therapy for patients who are not achieving PPG goals despite maximizing mealtime insulin doses.**

4- Injectable Amylin Analogues (Pramlintide)

- **Dose:**

  (Prandial insulin dose should be decrease 30-50%)

  - **Type1 DM:15 mcg S.C prior to meals, and can be titrated up in 15-mcg increments to a maximum of 60 mcg prior to each meal if tolerated and warranted.**
  - **Type 2 DM: 60 mcg S.C prior to meals, and may be titrated to the maximally recommended 120-mcg dose as tolerated and warranted**

- **S/Es: nausea, vomiting, anorexia**

5- Sulfonylureas:

Efficacy:	**High**
Drugs Names:	**1st generation agents seldom used today (e.g., chlorpropamide, tolbutamide)** **2nd generation agents (e.g., glyburide, glipizide, glimepiride).**
Hypoglycemia:	**Yes**
Weight change:	**Gain**
CV effects:	**Neutral**
Renal effects:	**Neutral**
Renal adjustment:	**All except tolbutamide, require dosage adjustment or are not recommended in renal impairment.**
Additional consideration:	**CV mortality (warring)**

5- Sulfonylureas:

- **Mechanism of Action:** **Bind to receptors on pancreatic β-cells, leading to membrane depolarization, with subsequent stimulation of insulin secretion (insulin secretagogue)**

- **Second-Generation Sulfonylurea Dosing Strategies dosage can be titrated every 1 to 2 weeks**

Drug	Initial Dosage	Maximum Daily Dosage (mg)
Glyburide (not micronized)	2.5–5.0 mg once or twice daily	20
Glyburide (micronized)	1.5–3 mg once or twice daily	12
Glipizide	5 mg once or twice daily (once daily with extended release)	40 (little improved efficacy > 20 mg/day)
Glimepiride	1–2 mg once daily	8

5- Sulfonylureas:

- Sulfonylureas typically reduce A1C by 1.5-2.0% and can cause weight gain of ~1-2 kg.

- S/Es: Hypoglycemia and weight gain (most common)

- Risk of hypoglycemia increase in
  - Elderly
  - Those with renal insufficiency
  - Advanced liver disease,
  - Those who skip meals
  - Exercise vigorously
  - Lose a substantial amount of weight

6- Meglitinides:

- Similar to sulfonylureas decrease glucose by stimulating pancreatic insulin secretion.
- BUT insulin elease is glucose dependent.
- A1Creduction 0.8% to 1%
- The drugs given before meal (up to 30 minutes prior)
- If meal skipped, the drugs should be skipped

- Repaglinide (Prandin)
  initiated at 0.5 to 2 mg with a maximum dose of 4 mg per meal (up to four meals per day or 16 mg/day).

- Nateglinide (Starlix)
  120 mg three times daily before each meal.
  60 mg per meal for patients who are near goal A1C

7- Biguanides:

Efficacy:	**High**
Drugs Names:	**metformin**
Hypoglycemia:	**No**
Weight change:	**Neutral (potential for modest loss)**
CV effects:	**Neutral HF, Benefit MACE**
Renal effects:	**Neutral**
Renal adjustment:	**Not recommended (CrCl <30)**
Additional consideration:	**GIT side effects & Lactic Acidosis**

MACE: Major adverse cardiovascular events

7- Biguanides:

- **Mechanism of Action:** **Reduces hepatic gluconeogenesis; also favorably affects insulin sensitivity and, to a lesser extent, intestinal absorption of glucose.**

- **Dosing**

  i. Initial: 500 mg once or twice daily (once daily with extended-release formulation)

  ii. Maximal daily dose: 2550 mg (more commonly, 2000 mg/day)

  iii. Can increase at weekly intervals as necessary

  iv. Small initial dosage and slow titration secondary to GI disturbances

7- Biguanides:

- **Metformin Efficacy**
  - **i. enhances insulin sensitivity,**
  - **ii. A1C reduction 1.5% to 2%,**
  - **iii. FPG reductions of 60 to 80 mg/dL,**
  - **iv. Decrease TG, LDL**
  - **v. Increase HDL**

- **S/Es:**
  - **. Abdominal discomfort, stomach upset, diarrhea, anorexia, and a metallic taste.**

- **Lactic acidosis (serious S/E) , so avoid it in patient with:**
  - **i. renal insufficiency**
  - **ii. tissue hypoperfusion states (HF, hepatic impairment)**

MACE: Major adverse cardiovascular events

8- Thiazolidinedione: (often called glitazones or TZDs):

Efficacy:	**High**
Drugs Names:	**Pioglitazone, Rosiglitazone**
Hypoglycemia:	**No**
Weight change:	**Gain**
CV effects:	**Worse HF, Benefit MACE (pioglitazone)**
Renal effects:	**Neutral**
Renal adjustment:	**No dose adjustment (precaution)**
Additional consideration:	**increase risk of fracture, increased risk for bladder cancer**

MACE: Major adverse cardiovascular events

8- Thiazolidinedione:

Thiazolidinediones: Dosing and Indications

DRUG	INDICATIONS	DOSING
Pioglitazone *Actos*	Improved glycemic control in T2DM	**Initial Dosing:** 15 mg to 30 mg PO once daily *A lower initial dose of 15 mg recommended in patients with congestive HF (NYHA class I or II)* **Max Dosing:** 45 mg daily **Titration:** May increase dose in 15 mg increments according to glycemic control
Rosiglitazone *Avandia*	Improved glycemic control in T2DM	**Initial Dosing:** 4 mg PO daily *(as single or two divided doses)* **Max Dosing:** 8 mg daily **Titration:** After 8-12 weeks, the dose may be increased to 8 mg daily for added glycemic control

8- Thiazolidinedione:

- **Mechanism of Action:**
  i. Activate peroxisome proliferator activator receptor-γ (PPAR-γ) → enhance insulin sensitivity
  ii. Increases expression of genes responsible for glucose metabolism, resulting in improved insulin sensitivity

- **Thiazolidinedione Efficacy**
  i. A1C reduction 1.5%
  ii. FPG reductions of 60 to 70 mg/dL

- **At least 3 to 4 months needed to reach maximum glycemic effects**
- **S/Es: Edema, weight gain, and hepatotoxicity**
- **They should be avoided in HF patients (C)**
- **TZDs are considered second- or third-line agents**

9- DPP-4 Inhibitors: (often called gliptin):

Efficacy:	**Intermediate**
Drugs Names:	**Alogliptin, linagliptin, saxagliptin, and sitagliptin**
Hypoglycemia:	**No**
Weight change:	**Neutral**
CV effects:	**Worsening HF (saxagliptin),neutral MACE**
Renal effects:	**Neutral**
Renal adjustment:	**Dose adj. required (Ex linagliptin)**
Additional consideration:	**Pancreatitis**

MACE: Major adverse cardiovascular events

9- DPP-4 Inhibitors: :

- **Mechanism of Action: Inhibit the breakdown of GLP-1 secreted during meals, which in turn increases pancreatic insulin secretion, limits glucagon secretion, slows gastric emptying, and promotes satiety**

- **DPP-4 Inhibitors Efficacy A1C reduction 0.7% to 1%**

- **S/Es: well tolerated; stuffy, runny nose, headache, URTI**

- **The BG-lowering effect of gliptins is primarily on postprandial levels.**

- **DPP-4 inhibitors are considered second- or third-line therapy**

DPP-4 Inhibitors: Dosing and Indications :

DRUG	INDICATIONS	DOSING	RENAL DOSING	HEPATIC DOSING
Alogliptin *Nesina*	Improved glycemic control in T2DM	**Initial Dosing:** 25 mg PO once daily *(dosed renally)* **Max Dosing:** 6.25 mg to 25 mg daily *(dependent on renal function)*	CrCl 30 to < 60 mL/min: 12.5 mg once daily CrCl < 30 mL/min: 6.25 mg once daily Hemodialysis: 6.25 mg once daily *(administer without regard to timing of hemodialysis)*	Mild to moderate impairment: No dose adjustment necessary Severe impairment: Insufficient data **Pharmacokinetics Pearl:** *Alogliptin is not extensively metabolized and drug levels are not expected to be meaningfully impacted (use with caution)*
Linagliptin *Tradjenta*	Improved glycemic control in T2DM	**Initial Dosing:** 5 mg PO once daily **Max Dosing:** 5 mg daily	No dose adjustment necessary	No dose adjustment necessary
Saxagliptin *Onglyza*	Improved glycemic control in T2DM	**Initial Dosing:** 2.5 mg to 5 mg PO once daily *(dosed renally)* **Max Dosing:** 2.5 mg to 5 mg daily *(dependent on renal function)*	eGFR < 45 mL/min: 2.5 mg once daily Hemodialysis: 2.5 mg once daily *(administer after hemodialysis)*	No dose adjustment necessary
Sitagliptin *Januvia*	Improved glycemic control in T2DM	**Initial Dosing:** 100 mg PO once daily *(dosed renally)* **Max Dosing:** 25 mg to 100 mg daily *(dependent on renal function)*	eGFR 30 mL/min to <45 mL/min: 50 mg once daily eGFR < 30 mL/min: 25 mg once daily Dialysis: 25 mg once daily *(administer without regard to timing of dialysis)*	Mild to moderate impairment: No dose adjustment necessary Severe impairment: Insufficient data **Pharmacokinetics Pearl:** *Sitagliptin is not extensively metabolized and drug levels are not expected to be meaningfully impacted (use with caution)*

The combined use of **GLP-1 RAs, tirzepatide** (GLP-1/GIP RA) and/or **DPP-4 inhibitors** is **not recommended** due to their similar mechanism of action.

10- sodium-dependent glucose cotransporter-2 inhibitor (SGLT-2 inhibitor)

Efficacy:	**Intermediate to high**
Drugs Names:	**Canagliflozin, Dapagliflozin, Empagliflozin, Ertugliflozin**
Hypoglycemia:	**No**
Weight change:	**Loss**
CV effects:	**Benefit MACE, benefit HF**
Renal effects:	**Benefit**
Renal adjustment:	**Dose adj. required**
Additional consideration:	**Increase risk of DKA**

10 - SGLT-2 inhibitor:

- **Mechanism of Action:** Increases urinary glucose excretion by blocking normal reabsorption in the proximal convoluted tubule; has some effect on delaying GI glucose absorption
- **S/Es:** Urinary tract infections (UTI), polyuria,↑ Creatinine (transient), Ketoacidosis

❖ SGLT-2 Inhibitors Efficacy:

i. 0.3%–1.0% reduction in A1C
ii. Effect on both fasting and postprandial glucose concentrations
iii. Mild weight loss
iv. Empagliflozin, dapagliflozin, and canagliflozin can reduce cardiovascular morbidity in patients with T2D and established cardiovascular disease and may improve renal outcomes.
v. Canagliflozin or dapagliflozin in patients with significant urine albumin excretion and renal insufficiency reduces the risk of end-stage renal disease, doubling of SCr, or renal death.
vi. All agents within the class have been shown to reduce heart failure admissions in patients with T2D with or without a history of heart failure.

SGLT-2 Inhibitors: Dosing and Indications :

DRUG	INDICATIONS	DOSING	RENAL DOSING	HEPATIC DOSING
Bexagliflozin *Brenzavvy*	T2DM: improved glycemic control	**Initial Dosing:** 20 mg PO once daily in the morning **Max Dosing:** 20 mg daily	eGFR < 30 mL/min: • Not recommended Dialysis: Use is contraindicated	Mild to moderate impairment: No dose adjustment necessary Severe impairment: Not studied, not recommended
Canagliflozin *Invokana*	T2DM: improved glycemic control Cardiovascular risk reduction *(in patients with T2DM & established CVD)* Renal risk reduction *(in patients with T2DM & diabetic nephropathy)*	**Initial Dosing:** 100 mg PO once daily *(take before 1st meal of the day)* **Max Dosing:** 300 mg daily **Titration:** May increase to 300 mg daily for added glycemic control	eGFR < 60 mL/min: Limit to 100 mg daily eGFR < 30 mL/min: • Initiation not recommended • Not recommended for glycemic control • May continue at 100 mg daily for renal risk reduction Dialysis: Use is contraindicated	Mild to moderate impairment: No dose adjustment necessary Severe impairment: Not studied, not recommended
Dapagliflozin *Farxiga*	T2DM: improved glycemic control Heart failure risk reduction *(in patients with or without T2DM)* Renal risk reduction *(in patients with CKD with or without T2DM)*	**Initial Dosing:** • 5 mg PO once daily *(for glycemic control)* • 10 mg PO once daily *(for heart failure or renal risk reduction)* **Max Dosing:** 10 mg daily **Titration:** May increase to 10 mg daily for added glycemic control *(no titration for heart failure or renal risk reduction indications)*	eGFR < 45 mL/min: Not recommended for glycemic control eGFR < 25 mL/min: • Initiation not recommended • Use for other indications (e.g., heart failure, chronic kidney disease) may continue at 10 mg daily Dialysis: Use is contraindicated	No dose adjustment necessary However, use in severe impairment has not been studied *(use with caution)*
Empagliflozin *Jardiance*	T2DM: improved glycemic control Cardiovascular risk reduction *(in patients with T2DM & established CVD)* Heart failure risk reduction *(in patients with or without T2DM)* Renal risk reduction *(in patients with CKD with or without T2DM)*	**Initial Dosing:** 10 mg PO once daily in the morning **Max Dosing:** 25 mg daily **Titration:** May increase to 25 mg daily for added glycemic control	eGFR < 30 mL/min: • Not recommended for glycemic control • Insufficient data to specify dosing for CV risk reduction eGFR < 20 mL/min: • Insufficient data to specify dosing for HF/CKD risk reduction Dialysis: Use is contraindicated	No dose adjustment necessary
Ertugliflozin *Steglatro*	T2DM: improved glycemic control	**Initial Dosing:** 5 mg PO once daily in the morning **Max Dosing:** 15 mg daily **Titration:** May increase to 15 mg daily for added glycemic control	eGFR < 45 mL/min: Use not recommended Dialysis: Use is contraindicated	Mild to moderate impairment: No dose adjustment necessary Severe impairment: Not studied, not recommended

11-Glucosidase inhibitors Acarbose & Miglitol

- **Mechanism of action: Slows the absorption of glucose from the intestine to the bloodstream by slowing the breakdown of large carbohydrates into smaller absorbable sugars**
- **A1C reduction 0.3% to 1%**
- **Good candidates: patients who are near target A1C levels with high postprandial levels**
- **S/Es: flatulence, bloating, abdominal discomfort, and diarrhea.**
- **Be careful for hypoglycemia management**
- **Dose: 25 mg/ day with meal, then increased very gradually (over several months) to (MAX 50 or 100mg three timedaily) taken with the first bite of the meal**

12- An others Agents:

1) Bile acid sequestrant

- Colesevelam (only approved for type 2 DM)
- MOA: unknown
- A1C reduction 0.4% when added to other essential regimens
- S/Es: GIT
- Dose: 3 tablets of 625-mg 2 times a day with meals

12- An others Agents:

2) Dopamine Receptor D2 Agonist:

- **Bromocriptine mesylate**
- **MOA: unknown (may increase insulin sensitivity)**
- **S/Es: Nausea, rhinitis, headache, asthenia, dizziness, constipation, and sinusitis**
- **A1C reduction 0.1 %to 0.4%**
- **Dose: 0.8-mg tablets administered within 2 hours of waking from sleep daily.**
  . Dose may increase weekly by 0.8 mg (MAX 4.8mg)
  . Effective dose: 1.6 mg to 4.8 mg

T2DM Drug Class Comparison

T2DM Drug Class	Mechanism	Route	A1C Lowering*	Hypoglycemia Risk	Weight Effect*	Cost
Biguanides (metformin)	Decreases hepatic production of glucose; increases insulin sensitivity	Oral	●●●	No	Potential for weight loss	$
SGLT2 inhibitors	Increases urinary glucose excretion	Oral	●●	No	Weight loss	$$$
GLP-1 receptor agonists	Increases glucose-dependent insulin release; decreases glucagon secretion; slows gastric emptying	SQ/Oral	●●●● **	No	Weight loss**	$$$$
GLP-1/GIP receptor agonists (e.g. tirzepatide)	Increases glucose-dependent insulin release; decreases glucagon secretion; slows gastric emptying	SQ	●●●●●	No	Weight loss	$$$$$
DPP-4 inhibitors	Increases glucose-dependent insulin release; decreases glucagon secretion	Oral	●	No	Neutral	$$$
Thiazolidinediones	Increases insulin sensitivity in muscle, fat and liver cells; increases glucose entry into cells	Oral	●●	No	+ Weight gain	$^
Sulfonylureas	Stimulates insulin secretion from pancreatic beta cells	Oral	●●●	Yes	+ Weight gain	$
Insulin Analogs	Stimulates peripheral glucose uptake by skeletal muscle and fat tissue; inhibits hepatic glucose production	SQ	●●●●● Titrate to response	Yes	+++ Weight gain	$$$
Human Insulin		SQ/Inhaled				$

T2DM Drug Class Comparison

DRUG/CLASS	ASCVD EFFECT	HF EFFECT	RENAL EFFECT	RENAL DOSING/USE*
Metformin Oral	Potential benefit	Neutral	Neutral	Contraindicated with eGFR < 30 mL/min
SGLT2is† Oral	**FDA approved for CVD benefit:** • canagliflozin • empagliflozin **Neutral:** • bexagliflozin** • dapagliflozin • ertugliflozin	**FDA approved for HF benefit:** • dapagliflozin • empagliflozin **Evidence for benefit:** • canagliflozin • ertugliflozin	**FDA approved:** • canagliflozin (DKD benefit) • dapagliflozin (CKD benefit) • empagliflozin (CKD benefit) **Neutral:** • bexagliflozin** • ertugliflozin	Renal dose adjustments necessary
GLP-1 RAs§ SUBQ injection *(except oral semaglutide)*	**FDA approved for CVD benefit:** • dulaglutide • liraglutide • semaglutide (SUBQ) **Neutral:** • exenatide ER • semaglutide (oral)	Neutral	**Evidence for benefit:** • dulaglutide • liraglutide • semaglutide (SUBQ)	Renal dose adjustments necessary for exenatide Not necessary for dulaglutide, liraglutide, or semaglutide (oral and SUBQ); however, monitoring for adverse effects is warranted

T2DM Drug Class Comparison

DRUG/CLASS	ASCVD EFFECT	HF EFFECT	RENAL EFFECT	RENAL DOSING/USE*
DPP-4is Oral	Neutral	**Potential risk** • saxagliptin	Neutral	Renal dose adjustments necessary for alogliptin, saxagliptin and sitagliptin Not necessary for linagliptin
TZDs Oral	**Potential CVD benefit:** • pioglitazone	**Increased risk:** • FDA boxed warning for congestive heart failure	Neutral	Renal dose adjustments not necessary Generally not recommended in renal impairment due to the potential for fluid retention
Sulfonylureas (2nd generation) Oral	Neutral	Neutral	Neutral	Glyburide: Generally not recommended in renal impairment Glimepiride, glipizide: Use lower initial dosing and titrate carefully
Insulin Analogs SUBQ injection **Human Insulin** SUBQ injection, inhaled	Neutral	Neutral	Neutral	Caution: Lower insulin doses necessary with decreased renal function Titrate according to clinical response

Section 5

Glycemic Goals and Hypoglycemia

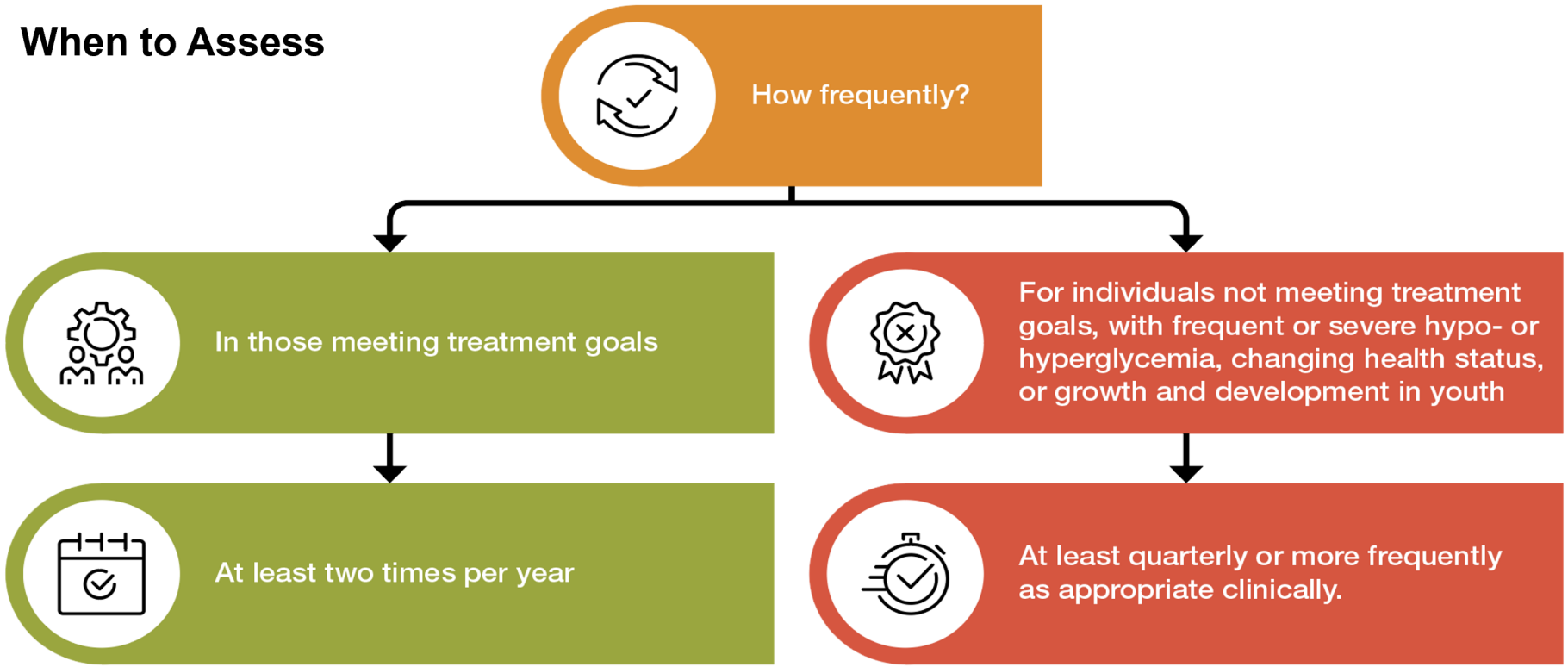
By: Dr. Rezg Yousef Al-Sunah
Bachelor of Clinical Pharmacy- Pharm-D

Assessment of Glycemic Status

How to Assess

- A1C measurement
- Continuous glucose monitoring (CGM) using appropriate metrics (e.g., time in range [TIR] and/or glucose management indicator [GMI])

When to Assess


How frequently?
In those meeting treatment goals
At least two times per year
For individuals not meeting treatment goals, with frequent or severe hypo- or hyperglycemia, changing health status, or growth and development in youth
At least quarterly or more frequently as appropriate clinically.

Assessment of Glycemic Status

Clinical Notes

Limitations:

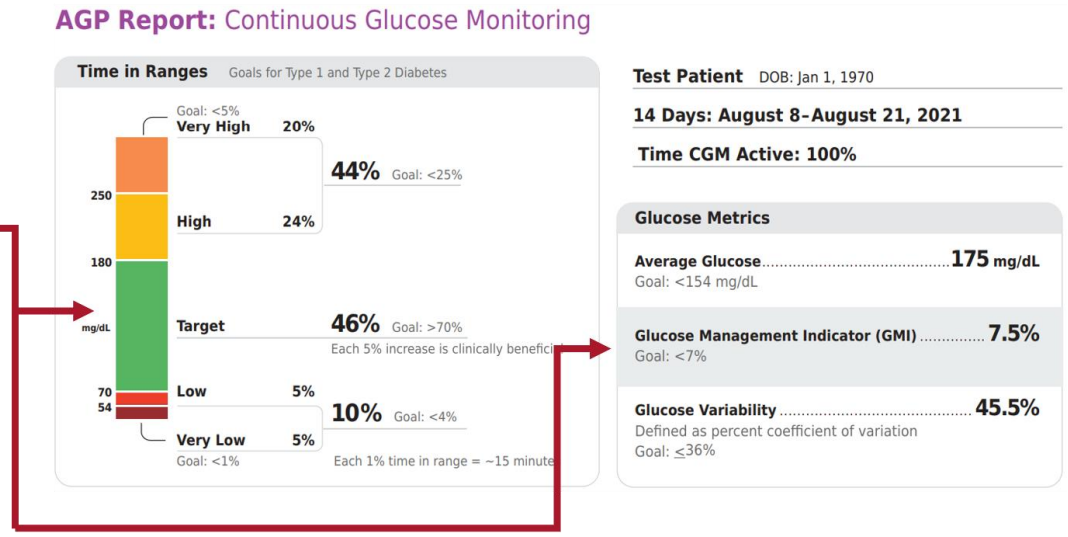
- Accuracy can be affected by conditions that affect red blood cell turnover (e.g., hemolytic and other anemias, glucose-6-phosphate dehydrogenase deficiency, recent blood transfusion, use of drugs that stimulate erythropoiesis, end-stage kidney disease, and pregnancy).
- Some hemoglobin variants can interfere with some A1C assays, although this problem has been minimized with newer assays.
- A1C does not assess glycemic variability or hypoglycemia.

Consider alternative measures, such as fructosamine and glycated albumin, when necessary.

Assess glycemic variability using a combination of results from blood glucose monitoring/CGM and A1C.

Glucose Assessment via CGM: The Ambulatory Glucose Profile (AGP) Report

1. Ensure sufficient data for analysis; CGM active at least 70% of the time over 14 days is recommended.
2. Discuss individuals' daily self-management routine.
3. Ask individuals to identify and explain what they observe on the report.
4. Check overall CGM metrics:
    - Time below range (TBR): percentage of readings and time with glucose <70 mg/dL (<3.9 mmol/L)
    - TIR: percentage of readings and time with glucose 70–180 mg/dL (3.9–10.0 mmol/L)
    - Time above range (TAR): percentage of readings and time >250 mg/dL (>13.9 mmol/L)
    - Mean glucose
    - Glucose management indicator (GMI): an estimate of A1C
    - Glycemic variability: expressed as percent coefficient of variation; target ≤36%



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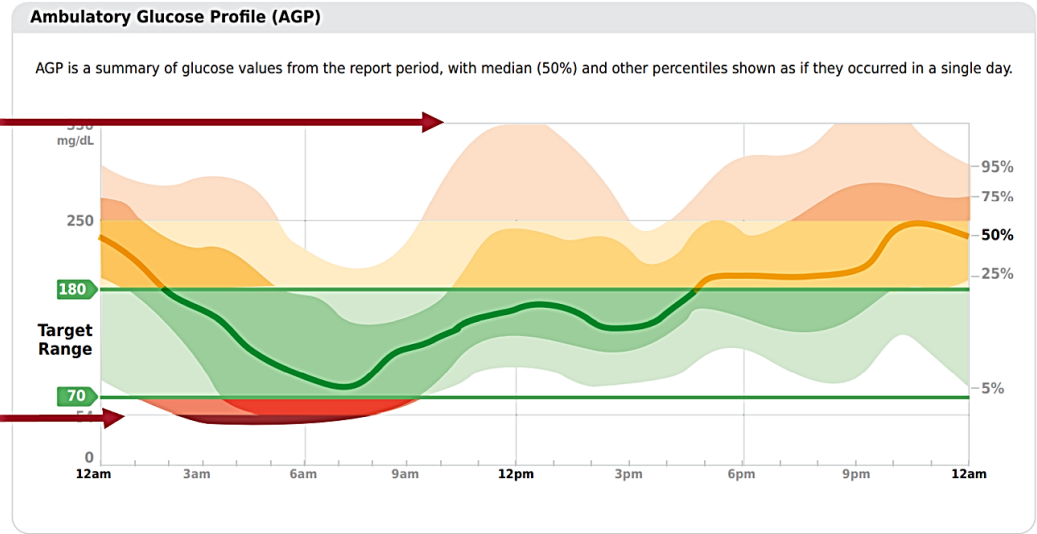
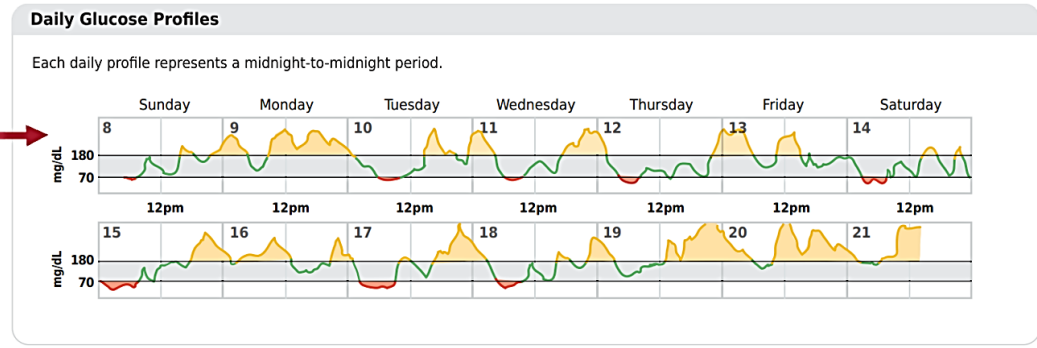
Glucose Assessment via CGM: The Ambulatory Glucose Profile (AGP) Report

5. Identify any hypoglycemia first, and then look for hyperglycemia patterns. Review the time spent in these patterns on the overall profile and daily graphs.
6. Discuss identified patterns and ask individuals to reflect on potential causes and possible solutions.
7. If you use CGM metrics to assess glycemia, goals for nonpregnant adults or those with frailty will vary; set glycemic goals based on the general guidelines below.
8. Use shared decision-making to develop an action plan.





Correlation Between A1C and Estimated Average Glucose (eAG)

A calculator for converting A1C results into eAG, in either mg/dL or mmol/L, is available at professional.diabetes.org/eAG.

Data in parentheses are a 95% CI.

- **eAG (mg/dL) = 28.7 × HbA1C% - 46.7**
- **eAG (mg/mmol) = 1.59 × HbA1C% - 2.59**

A1C (%)	mg/dL	mmol/L
5	97 (76–120)	5.4 (4.2–6.7)
6	126 (100–152)	7.0 (5.5–8.5)
7	154 (123–185)	8.6 (6.8–10.3)
8	183 (147–217)	10.2 (8.1–12.1)
9	212 (170–249)	11.8 (9.4–13.9)
10	240 (193–282)	13.4 (10.7–15.7)
11	269 (217–314)	14.9 (12.0–17.5)
12	298 (240–347)	16.5 (13.3–19.3)

Adapted from Nathan DM, Kuenen J, Borg R, Zheng H, Schoenfeld D; A1c-Derived Average Glucose Study Group. Translating the A1C assay into estimated average glucose values. Diabetes Care 2008;31:1473–1478

Setting and Modifying Glycemic Goals

Glycemic goals should be individualized and periodically reevaluated.

1. Individualize based on key characteristics of the person with diabetes.

2. Individualize in the context of shared decision-making (to address needs and preferences).

3. Follow these general guidelines:

- Recommended glycemic goals for many nonpregnant adults with diabetes without significant hypoglycemia:
  - A1C <7.0% (<53 mmol/mol)
  - Preprandial capillary plasma glucose: 80–130 mg/dL (4.4–7.2 mmol/L)
  - Peak postprandial capillary plasma glucose: <180 mg/dL (<10.0 mmol/L)
  - CGM metrics: TIR >70% with TBR <4% and <1% of time with glucose <54 mg/dL
- A lower A1C goal may be acceptable and even beneficial if it can be achieved safely without significant hypoglycemia or other adverse effects of treatment.
- A higher A1C goal (such as <8% [64 mmol/mol]) may be appropriate for individuals with limited life expectancy or when the harms of treatment are greater than the benefits.
- TIR >50% with <1% TBR is appropriate in those with frailty or at high risk of hypoglycemia.
- Deintensify glucose-lowering medications for those at high hypoglycemia risk or when treatment risks or burdens outweigh the benefits.

Approach to Individualization of Glycemic Targets

Patient/Disease Features	More Stringent < A1C 7% > Less Stringent
Risks potentially associated with hypoglycemia and other drug-related adverse effects	Low — High
Disease Duration	Newly Diagnosed — Long Standing
Life expectancy	Long — Short
Important comorbidities	Absent — few/mild — Severe
Established vascular complications	Absent — few/mild — Severe
Individual needs and preference	Highly motivated, excellent self-care capabilities — Preference for less burdensome therapy
Resources and support system	Readily Available — Limited

Person and disease factors used to determine optimal glycemic targets. Characteristics and predicaments toward the left justify more stringent efforts to lower A1C; those toward the right suggest less stringent efforts. A1C 7% = 53 mmol/mol.

Section 6
Type-1 DM Treatment

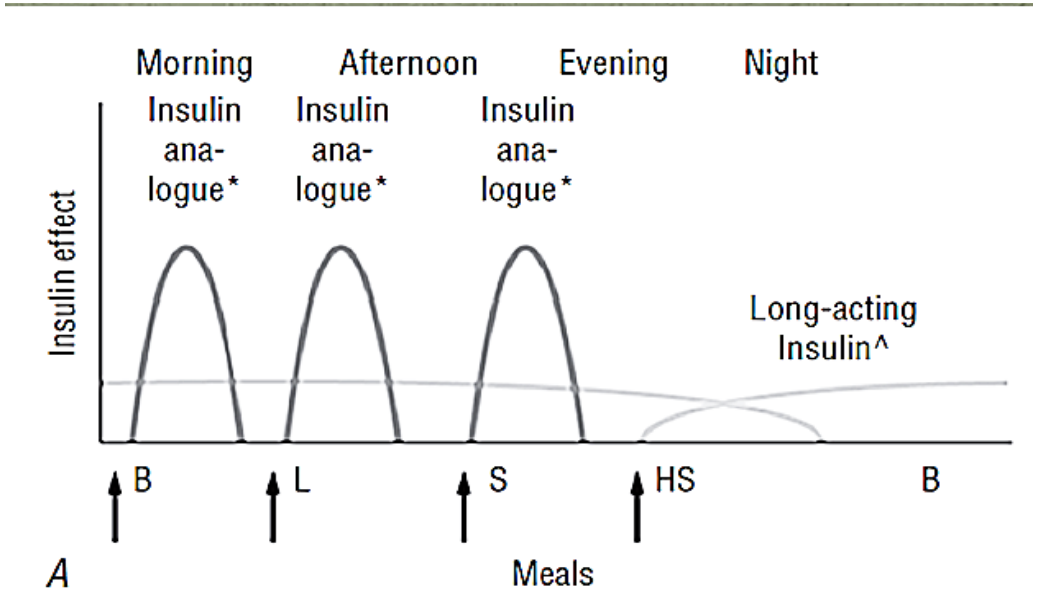
By: Dr. Rezg Yousef Al-Sunah
Bachelor of Clinical Pharmacy- Pharm-D

Type-1 DM Treatment

- All patients with type I DM require insulin.
- Type-1 DM require 0.4 to 1 unit/kg/day, but the type and manner of delivery are different . The typical starting dose for T1DM is 0.5 units/kg/day
- Therapeutic strategies should attempt to match carbohydrate intake with insulin and exercise.
- Pramlintide indicated in type 1 DM patients who are not achieving glycemic targets despite optimization of mealtime insulin.

Type-1 DM Treatment

- **A common multiple daily injections (MDI) approach:**
  - **One injection of long-acting insulin (basal)**
  - **Three injections of rapid-acting insulin (bolus or prandial)**



STARTING A BASAL-BOLUS INSULIN REGIMEN IN TYPE 1 DIABETES

- Insulin is dosed using total body weight (TBW).
- Commonly, 50% of the total daily dose (TDD) is administered as basal insulin and 50% as prandial (bolus) insulin.
- Steps:

1. Calculate TDD (0.5 units/kg/day, using TBW)

2. Divide the TDD into 50% basal insulin and 50% bolus (rapid-acting) insulin

3. Divide the bolus insulin evenly among 3 meals (or allocate more insulin for larger meals and less for smaller meals).

CASE SCENARIO

Start a basal-bolus regimen with Lantus and Humalog in a patient with type 1 diabetes that weighs 84 kg,

1. Calculate the TDD:
0.5 units/kg/day X 84 kg = 42 units

2. Split the dose in half for basal and rapid-acting insulin:
21 units Lantus and 21 units Humalog

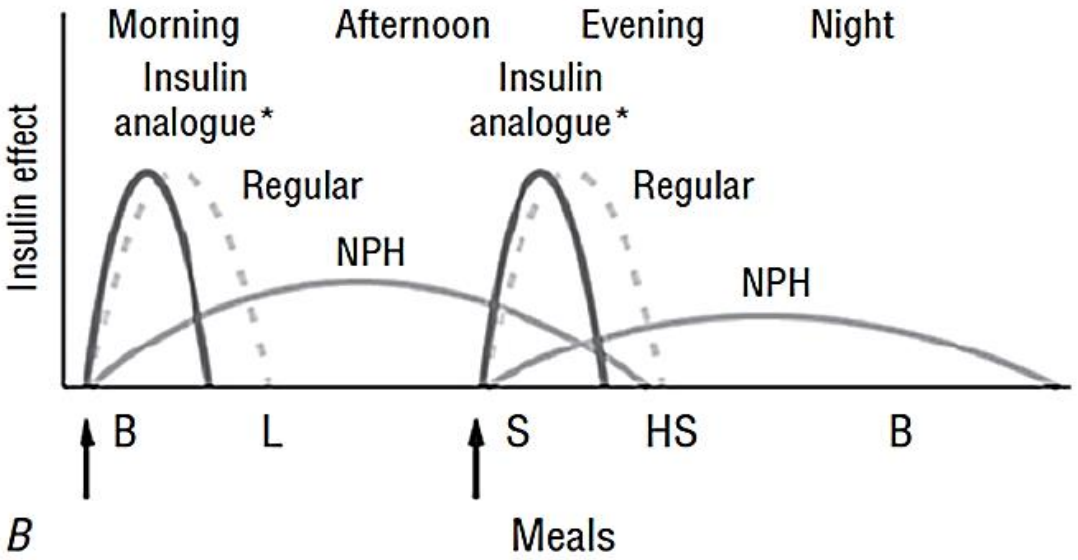
3. Split rapid-acting insulin into 3 even doses:
7 units Humalog TID AC

Answer: 21 units Lantus daily and 7 units Humalog TID AC

Type-1 DM Treatment

- **Another multiple daily injections (MDI) approach:**

- **Two injections of intermediate-acting insulin**
- **Two injections of short-acting insulin**



CORRECTION DOSES FOR ELEVATED BLOOD GLUCOSE

1) **The first step is to calculate the correction factor, which indicates how much the BG will be lowered (in mg/dL) by 1 unit of insulin**

Correction Factor – 1,500 Rule *for REGULAR*

$$\frac{1{,}500}{\text{total daily dose of insulin (TDD)}} = \text{correction factor for 1 unit of regular insulin}$$

Correction Factor – 1,800 Rule *for RAPID-ACTING*

$$\frac{1{,}800}{\text{total daily dose of insulin (TDD)}} = \text{correction factor for 1 unit of rapid-acting insulin}$$

1) **Next, calculate the correction dose,**

Calculate the Correction Dose *BOTH TYPES*

$$\frac{\text{(blood glucose now) – (target blood glucose)}}{\text{correction factor}} = \text{correction dose}$$

CASE SCENARIO

JJ is a 35-year-old male with T2D, currently treated with Lantus 50 units SC QD and Novolog 15 units SC TID AC.

1. What is JJ's correction factor?
2. JJ has a target premeal BG of 120 mg/dL. He checks his BG before dinner and it is 200 mg/dL. What dose of Novolog should JJ administer before dinner?

Type-1 DM Treatment

- **Comparing of Injectable insulin regimens**

Injected insulin regimens	Flexibility	Lower risk of hypoglycemia	Higher costs
MDI with LAA + RAA or URAA	+++	+++	+++
Less-preferred, alternative injected insulin regimens			
MDI with NPH + RAA or URAA	++	++	++
MDI with NPH + short-acting (regular) insulin	++	+	+
Two daily injections with NPH + short-acting (regular) insulin or premixed	+	+	+

Section 7

Treatment of Hyperglycemia in Type 2 Diabetes

By: Dr. Rezg Yousef Al-Sunah
Bachelor of Clinical Pharmacy- Pharm-D

Type-2 DM Treatment

- **Upon diagnosis, assess the patient's current lifestyle, existing comorbidities, A1C, age, weight, presence or absence of symptoms, motivation, cultural preferences, health literacy level, and cost limitations. Set a patient-specific A1C target and discuss it with the patient.**

- **Implement comprehensive lifestyle modifications with MNT, physical activity, weight loss if obese, smoking cessation, and psychologic support upon diagnosis and reinforce them at every visit.**
- **All patients should be offered access to ongoing DSME/S programs.**

Type-2 DM Treatment

- **If the initial A1C is close to the goal (eg, ≤7.5%) consider initial treatment with lifestyle modifications alone if the patient is motivated.**

- **Initiate metformin as first-line therapy in patients without contraindications or tolerability issues.**

- **Consider starting two medications (metformin plus a second agent) if the initial A1C is >1.5% higher than the target A1C.**

Type-2 DM Treatment

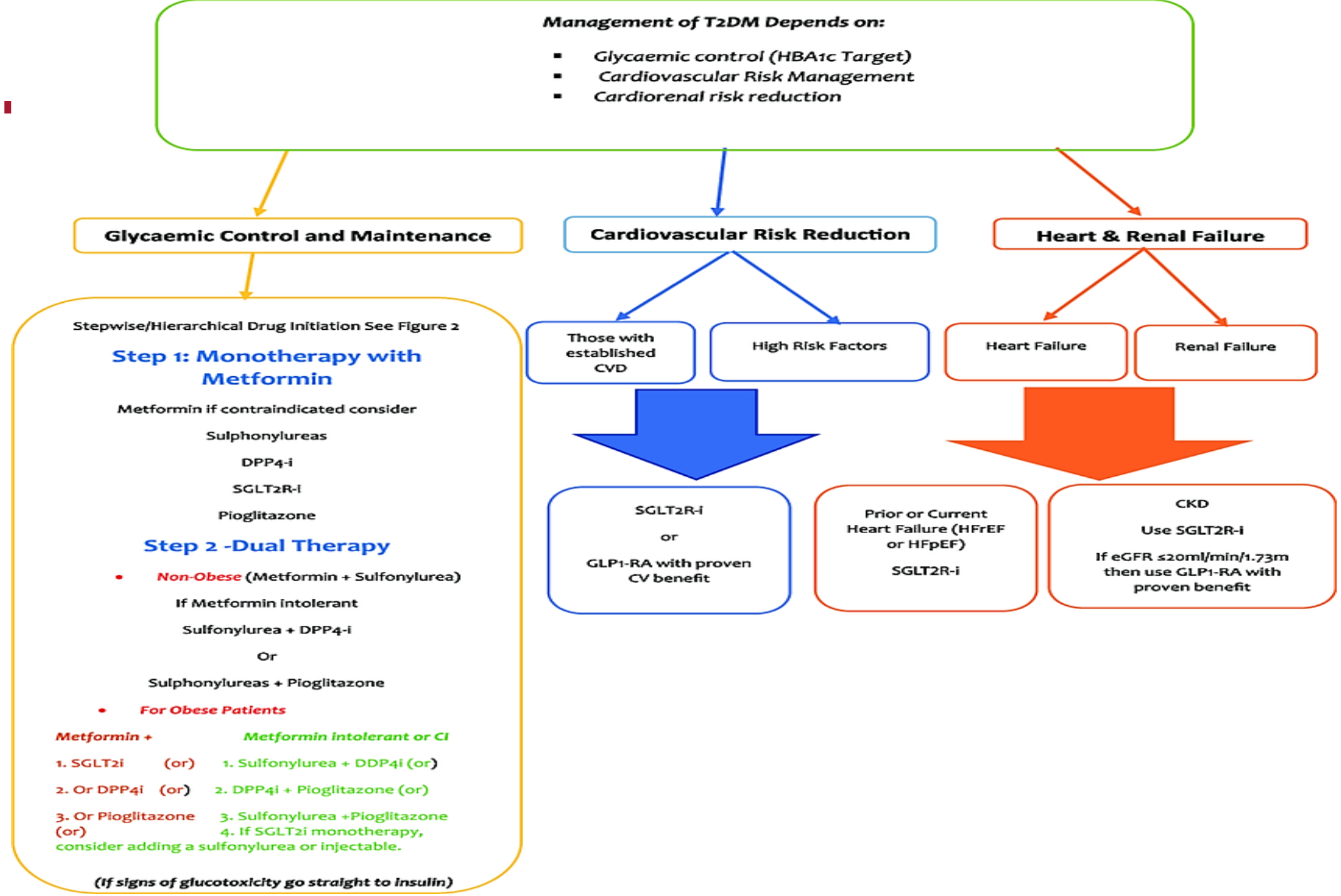
- **Consider early introduction of basal insulin in patients with:**
  i. Very high A1C levels >10%
  ii. Symptoms of hyperglycemia
  iii. Evidence of catabolism (eg, weight loss)

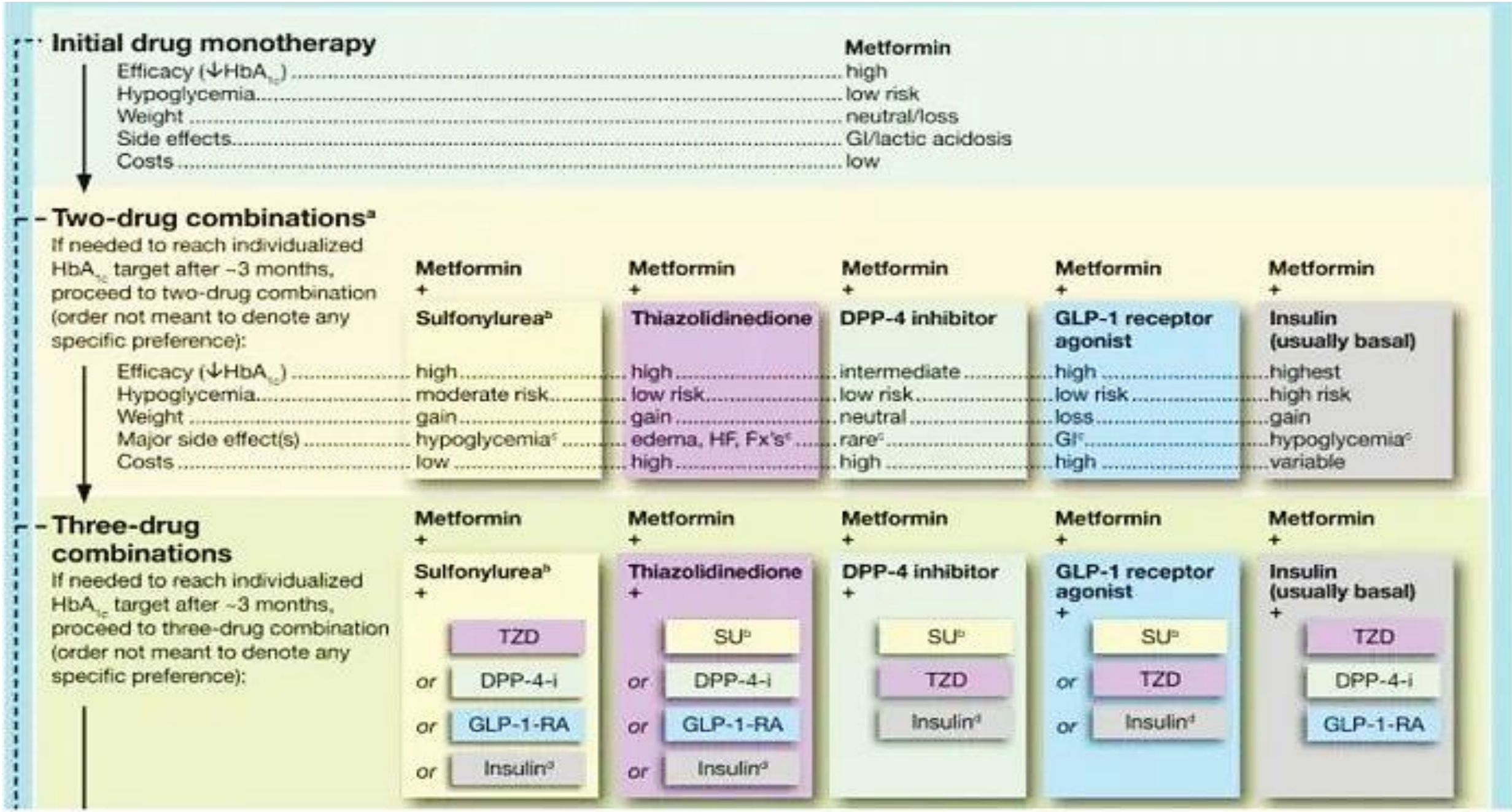
- **See patients at least every 3 months (not meeting goals) or at least every 6 months (meeting goals)**
- **At those times;**
  i. Check an A1C level
  ii. Assess medication adherence
  iii. Reinforce lifestyle recommendations
  iv. Add additional therapy if glucose targets have not been met.

Type-2 DM Treatment

- **For patients maximized on metformin therapy but with A1C levels above the target, add a second-line antihyperglycemic agent.**
- **The ADA Standards of Care identify six drug classes to consider:**
  - ✓ **DPP-4 inhibitors**
  - ✓ **GLP1-Ras**
  - ✓ **SGLT-2 inhibitors**
  - ✓ **Sulfonylureas**
  - ✓ **TZDs**
  - ✓ **Basal insulin**

❖ **Note: Patients with CVD or CKD (choose approved agents)**


Management of T2DM Depends on:
Glycaemic control (HBA1c Target)
Cardiovascular Risk Management
Cardiorenal risk reduction
Glycaemic Control and Maintenance
Cardiovascular Risk Reduction
Heart & Renal Failure
Stepwise/Hierarchical Drug Initiation See Figure 2
Step 1: Monotherapy with Metformin
Metformin if contraindicated consider
Sulphonylureas
DPP4-i
SGLT2R-I
Pioglitazone
Step 2 -Dual Therapy
Non-Obese (Metformin + Sulfonylurea)
If Metformin Intolerant
Sulfonylurea + DPP4-i
Or
Sulphonylureas + Pioglitazone
For Obese Patients
Metformin +
1. SGLT2i (or)
2. Or DPP4i (or)
3. Or Pioglitazone (or)
Metformin intolerant or CI
1. Sulfonylurea + DDP4i (or)
2. DPP4i + Pioglitazone (or)
3. Sulfonylurea +Pioglitazone
4. If SGLT2i monotherapy, consider adding a sulfonylurea or injectable.
(If signs of glucotoxicity go straight to insulin)
Those with established CVD
High Risk Factors
Heart Failure
Renal Failure
SGLT2R-i
or
GLP1-RA with proven CV benefit
Prior or Current Heart Failure (HFrEF or HFpEF)
SGLT2R-i
CKD
Use SGLT2R-i
If eGFR ≤20ml/min/1.73m then use GLP1-RA with proven benefit


Initial drug monotherapy
Metformin
Efficacy (↓HbA1c) high
Hypoglycemia low risk
Weight neutral/loss
Side effects GI/lactic acidosis
Costs low
Two-drug combinations[a]
If needed to reach individualized HbA1c target after ~3 months, proceed to two-drug combination (order not meant to denote any specific preference):
Metformin + Sulfonylurea[b]
Metformin + Thiazolidinedione
Metformin + DPP-4 inhibitor
Metformin + GLP-1 receptor agonist
Metformin + Insulin (usually basal)
Efficacy (↓HbA1c) high | high | intermediate | high | highest
Hypoglycemia moderate risk | low risk | low risk | low risk | high risk
Weight gain | gain | neutral | loss | gain
Major side effect(s) hypoglycemia[c] | edema, HF, Fx's[c] | rare[c] | GI[c] | hypoglycemia[c]
Costs low | high | high | high | variable
Three-drug combinations
If needed to reach individualized HbA1c target after ~3 months, proceed to three-drug combination (order not meant to denote any specific preference):
Metformin + Sulfonylurea[b] + TZD or DPP-4-i or GLP-1-RA or Insulin[d]
Metformin + Thiazolidinedione + SU[b] or DPP-4-i or GLP-1-RA or Insulin[d]
Metformin + DPP-4 inhibitor + SU[b] TZD Insulin[d]
Metformin + GLP-1 receptor agonist + SU[b] or TZD or Insulin[d]
Metformin + Insulin (usually basal) + TZD DPP-4-i GLP-1-RA

Use of Glucose-Lowering Medications in the Management of Type 2 Diabetes

HEALTHY LIFESTYLE BEHAVIORS; DIABETES SELF-MANAGEMENT EDUCATION AND SUPPORT (DSMES); SOCIAL DETERMINANTS OF HEALTH (SDOH)

TO AVOID THERAPEUTIC INERTIA REASSESS AND MODIFY TREATMENT REGULARLY (3–6 MONTHS)

Goal: Cardiorenal Risk Reduction in High-Risk Individuals with Type 2 Diabetes (in addition to comprehensive CV risk management)*

+ASCVD†

Defined differently across CVOTs but all included individuals with established CVD (e.g., MI, stroke, any revascularization procedure). Variably included: conditions such as transient ischemic attack, unstable angina, amputation, symptomatic or asymptomatic coronary artery disease.

+Indicators of high risk

While definitions vary, most comprise ≥55 years of age with two or more additional risk factors (including obesity, hypertension, smoking, dyslipidemia, or albuminuria)

+ASCVD/Indicators of High Risk

GLP-1 RA# with proven CVD benefit **EITHER/ OR** SGLT2i§ with proven CVD benefit

If A1C above target

- For patients on a GLP-1 RA consider adding SGLT2i with proven CVD benefit or vice versa
- TZD^

+HF

Current or prior symptoms of HF with documented HFrEF or HFpEF

+HF

SGLT2i§ with proven HF benefit in this population

+CKD

eGFR <60 mL/min per 1.73 m² OR albuminuria (ACR ≥3.0 mg/mmol [30mg/g]). These measurements may vary over time; thus, a repeat measure is required to document CKD.

+CKD (on maximally tolerated dose of ACEi/ARB)

PREFERABLY

SGLT2i§ with primary evidence of reducing CKD progression

Use SGLT2i in people with an eGFR ≥20 mL/min per 1.73 m²; once initiated should be continued until initiation of dialysis or transplantation

OR

GLP-1 RA with proven CVD benefit if SGLT2i not tolerated or contraindicated

If A1C above target, for patients on SGLT2i, consider incorporating a GLP-1 RA or vice versa

If additional cardiorenal risk reduction or glycemic lowering needed

Goal: Achievement and Maintenance of Glycemic and Weight Management Goals

Glycemic Management: Choose approaches that provide the efficacy to achieve goals:

Metformin OR Agent(s) including COMBINATION therapy that provide adequate EFFICACY to achieve and maintain treatment goals

Prioritize avoidance of hypoglycemia in high-risk individuals

In general, higher efficacy approaches have greater likelihood of achieving glycemic goals

Efficacy for glucose lowering

Very High:
Dulaglutide (high dose), Semaglutide, Tirzepatide

Insulin

Combination Oral, Combination Injectable (GLP-1 RA/Insulin)

High:
GLP-1 RA (not listed above), Metformin, SGLT2i, Sulfonylurea, TZD

Intermediate:
DPP-4i

Achievement and Maintenance of Weight Management Goals:

Set individualized weight management goals

General lifestyle advice: medical nutrition therapy/ eating patterns/ physical activity

Intensive evidence-based structured weight management program

Consider medication for weight loss

Consider metabolic surgery

When choosing glucose-lowering therapies:
Consider regimen with high-to-very-high dual glucose and weight efficacy

Efficacy for weight loss

Very High:
Semaglutide, Tirzepatide

High:
Dulaglutide, Liraglutide

Intermediate:
GLP-1RA (not listed above), SGLT2i

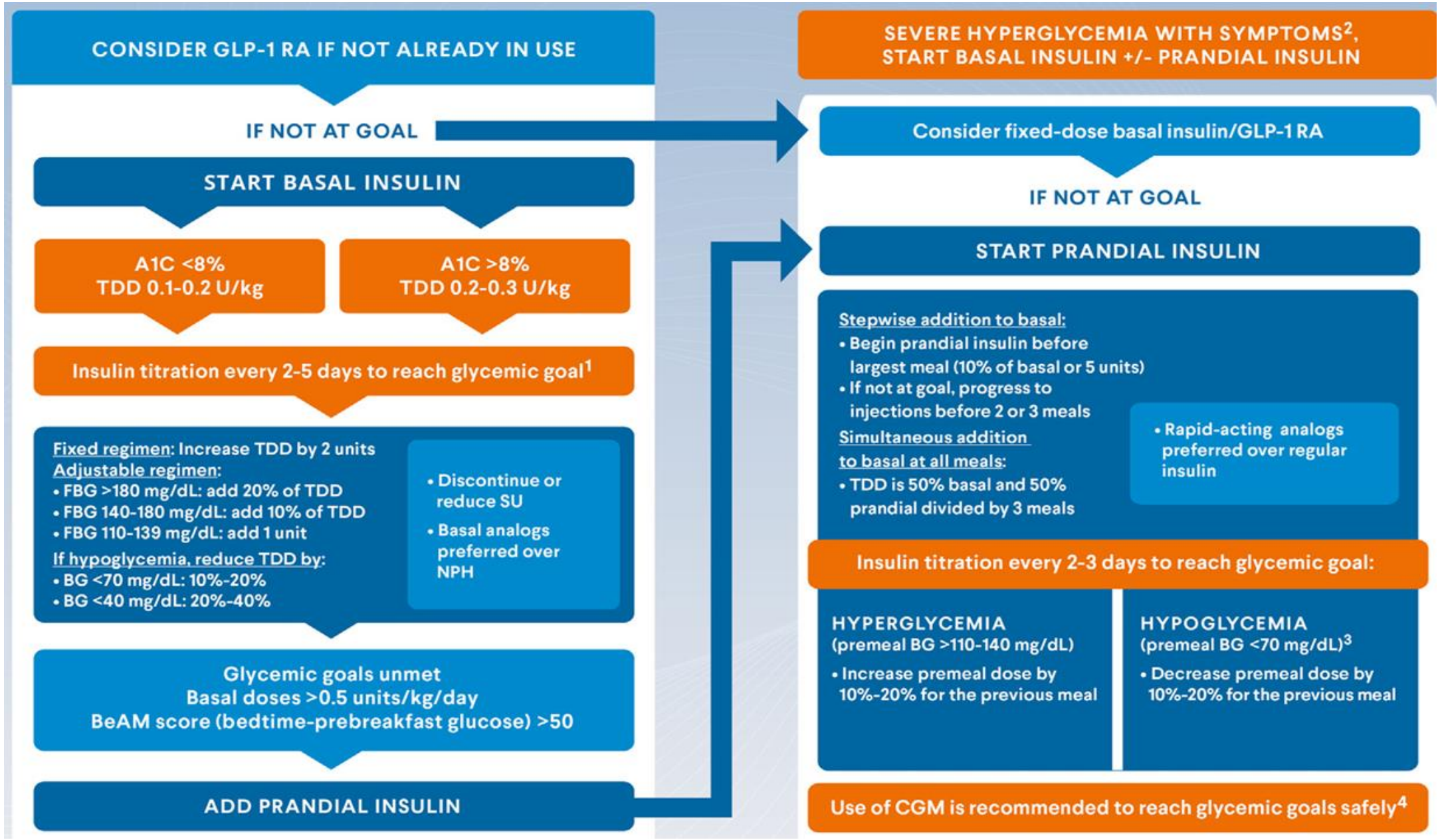
Neutral:
DPP-4i, Metformin

If A1C above target

Identify barriers to goals:

- Consider DSMES referral to support self-efficacy in achievement of goals
- Consider technology (e.g., diagnostic CGM) to identify therapeutic gaps and tailor therapy
- Identify and address SDOH that impact achievement of goals

Algorithm for Adding/Intensifying Insulin.



To-Do List for Clinicians Treating People With Insulin Therapy

- ❑ Provide or refer patients for education about injection technique and timing and problem-solving for issues related to insulin therapy (e.g., hypoglycemia, missed or incorrect doses, and dose adjustments).
- ❑ Ensure that individuals have all supplies necessary for injections (e.g., pen needles for insulin pens or appropriate syringes for insulin dose size or concentration) and glucose monitoring.
- ❑ Evaluate individuals with type 2 diabetes to determine whether they are candidates for GLP-1 or dual GIP/GLP-1 receptor agonist therapy.
- ❑ Evaluate all people on insulin therapy to determine whether they could benefit from continuous glucose monitoring.
- ❑ Ensure that people on insulin therapy have the education and supplies needed to prevent and treat hypoglycemia, including glucagon, glucose monitoring supplies, and appropriate sources of carbohydrates to treat low glucose levels.
- ❑ Schedule timely and routine follow-up visits to reassess patients and adjust care plans to avoid therapeutic inertia.

Section 8

Management of Diabetes Mellitus Complications

By: Dr. Rezg Yousef Al-Sunah
Bachelor of Clinical Pharmacy- Pharm-D

Treatment of Diabetes Mellitus Complications

1) Hypoglycemia
2) Diabetic Ketoacidosis
3) Nephropathy
4) Retinopathy
5) DM Neuropathies

1- Hypoglycemia Assessment, Prevention, and Treatment

Assessment and medication selection
Review hypoglycemia history at every clinical encounter in all at-risk individuals.
Screen for impaired hypoglycemia awareness in all at-risk individuals.
Consider hypoglycemia risk when selecting diabetes medications and setting glycemic goals.

1- Hypoglycemia Assessment, Prevention, and Treatment

1) **Mild to moderate hypoglycemia**

   i. Oral ingestion of 15–20 g of glucose or equivalent
   ii. Repeat glucose concentration in 15 minutes and, if still less than 70 mg/dL, repeat ingestion of glucose.
   iii. Once glucose is normalized, ingest snack or meal

2) **Clinically significant hypoglycemia (altered consciousness, needs assistance from others)**

   i. Glucagon 1 mg subcutaneously or intramuscularly or 3 mg by nasal inhalation
   ii. Intravenous dextrose if patient does not respond to glucagon
   iii. Raise glucose targets for several weeks

3- Diabetic Ketoacidosis Assessment.

1) More common in T1D but can occur in T2DM.

2) Usually occurs because of a precipitating factor that stresses the body, resulting in increased counter regulatory hormones
   a. Inappropriate (including nonadherence) or inadequate insulin therapy and infection are the two most common causes.
   b. Other causes: Myocardial infarction, pancreatitis, stroke, drugs (e.g., corticosteroids)

3) Results in significant hyperglycemia, dehydration, and ketoacidosis

4) Common signs and symptoms: Polyuria, polydipsia, vomiting, dehydration, weakness, altered mental status, coma, abdominal pain, Kussmaul respirations, tachycardia, hyponatremia, hyperkalemia

3- Diabetic Ketoacidosis Treatment

1) Treat underlying cause, if known.

2) Fluid replacement
   i. 0.45%–0.9% sodium chloride, depending on baseline serum sodium concentrations
   ii. Change to 5% dextrose with 0.45% sodium chloride when serum glucose is less than 200 mg/dL.

3) Insulin:
   i. Goal is to stop ketosis, not to normalize glucose concentrations.
   ii. Intravenous bolus regular insulin: 0.1 unit/kg
   iii. Intravenous infusion

0.1 unit/kg/hour regular insulin (increase if not a 50- to 75-mg/dL decrease in serum glucose in the first hour) Interrupt insulin treatment if baseline serum potassium is less than 3.3 mEq/L and until corrected.

Optimizing the management of glycemia, blood pressure, and lipids can reduce or slow the progression of microvascular complications of diabetes.

Diabetic Retinopathy (DR)

Screening

Recommended DR screenings can allow for timely treatment to prevent or reverse vision loss.

How?	When?	Follow-Up Eye Exam Schedule
Dilated comprehensive eye exam **Retinal photography***	**For people with type 1 diabetes: within 5 years after the onset of diabetes** **For people with type 2 diabetes: at the time of diabetes diagnosis**	▪ **At least annually for people with any level of retinopathy** ▪ **Every 1–2 years for those with no retinopathy for one or more annual exams and well-managed glycemia** ▪ **More frequently for those with progressing or sight-threatening retinopathy**

*Retinal photography with remote reading or use of an authorized artificial intelligence tool can expand access to screening where qualified eye care professionals are not available. When abnormalities are detected, in-person exams will be needed.

Diabetic Retinopathy (DR)

Treatment

Promptly refer to an ophthalmologist who is knowledgeable and experienced in managing DR any individuals with:

- Any level of diabetic macular edema
- Moderate or worse nonproliferative DR (a precursor of proliferative DR)
- Any proliferative DR

Neuropathy

Screening

All people with diabetes should be assessed for diabetic peripheral neuropathy (DPN):

- Starting at the diagnosis of type 2 diabetes
- 5 years after the diagnosis of type 1 diabetes
- At least annually thereafter

Symptoms and signs of autonomic neuropathy should be assessed:

- Starting at the diagnosis of type 2 diabetes
- 5 years after the diagnosis of type 1 diabetes
- At least annually thereafter
- With evidence of other microvascular complications, particularly kidney disease and DPN

Neuropathy

Neuropathic pain therapy

a. ADA recommendations consider duloxetine, gabapentin, or pregabalin as initial therapy.
b. Tricyclic antidepressants (amitriptyline, desipramine)
c. Anticonvulsants (gabapentin, lamotrigine, pregabalin)
d. Selective serotonin reuptake inhibitor/selective serotonin and norepinephrine reuptake inhibitor (duloxetine, paroxetine, citalopram, venlafaxine)
e. Tramadol/acetaminophen: As effective as gabapentin; different adverse effect profile
f. Opioids: Tapentadol extended release is the only approved agent in this class; no head-to-head efficacy studies

Foot Care

Initial treatment recommendations should include:

- Daily foot inspection
- Use of moisturizers for dry, scaly skin and avoidance of self-care of ingrown nails and calluses
- Well-fitted athletic or walking shoes with customized pressure-relieving orthoses for people with increased plantar pressures (e.g., with plantar calluses).

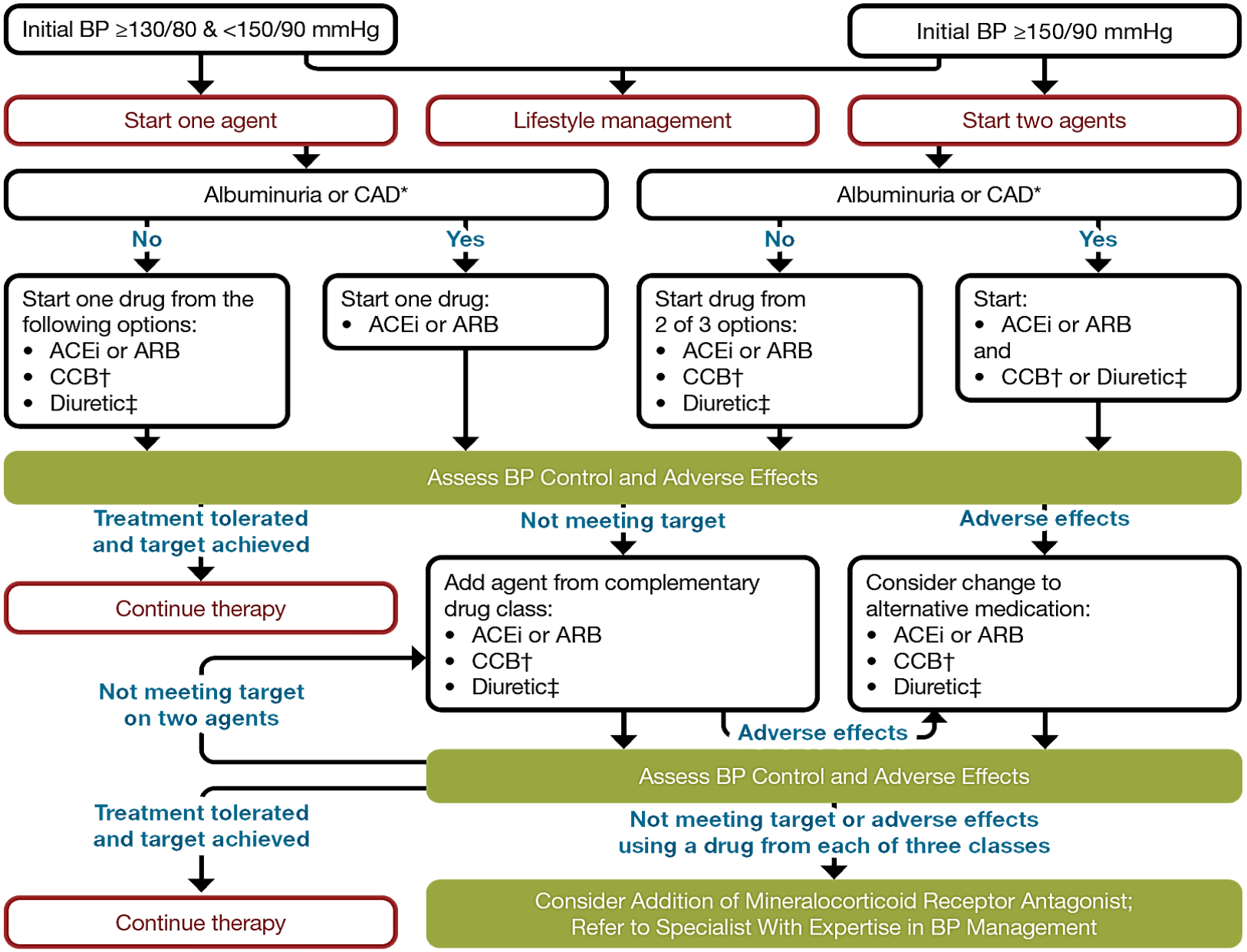
Foot Care

Risk Stratification and Screening Frequency

Category	Ulcer Risk	Characteristics	Examination Frequency
0	Very low	No LOPS and no PAD	Annually
1	Low	LOPS or PAD	Every 6–12 months
2	Moderate	LOPS + PAD, or LOPS/PAD + foot deformity	Every 3–6 months
3	High	LOPS or PAD and one or more of the following: ▪ History of foot ulcer ▪ Amputation (minor or major) ▪ End-stage renal disease	Every 1–3 months

Adapted with permission from Schaper NC, van Netten JJ, Apelqvist J, Bus SA, Hinchliffe RJ; IWGDF Editorial Board. Practical guidelines on the prevention and management of diabetic foot disease (IWGDF 2019 update). Diabetes Metab Res Rev 2020;36(Suppl. 1):e3266. LOPS, loss of protective sensation. PAD, peripheral artery disease. Examination frequency suggestions are based on expert opinion and person-centered requirements.

Cardiovascular Disease and Risk Management



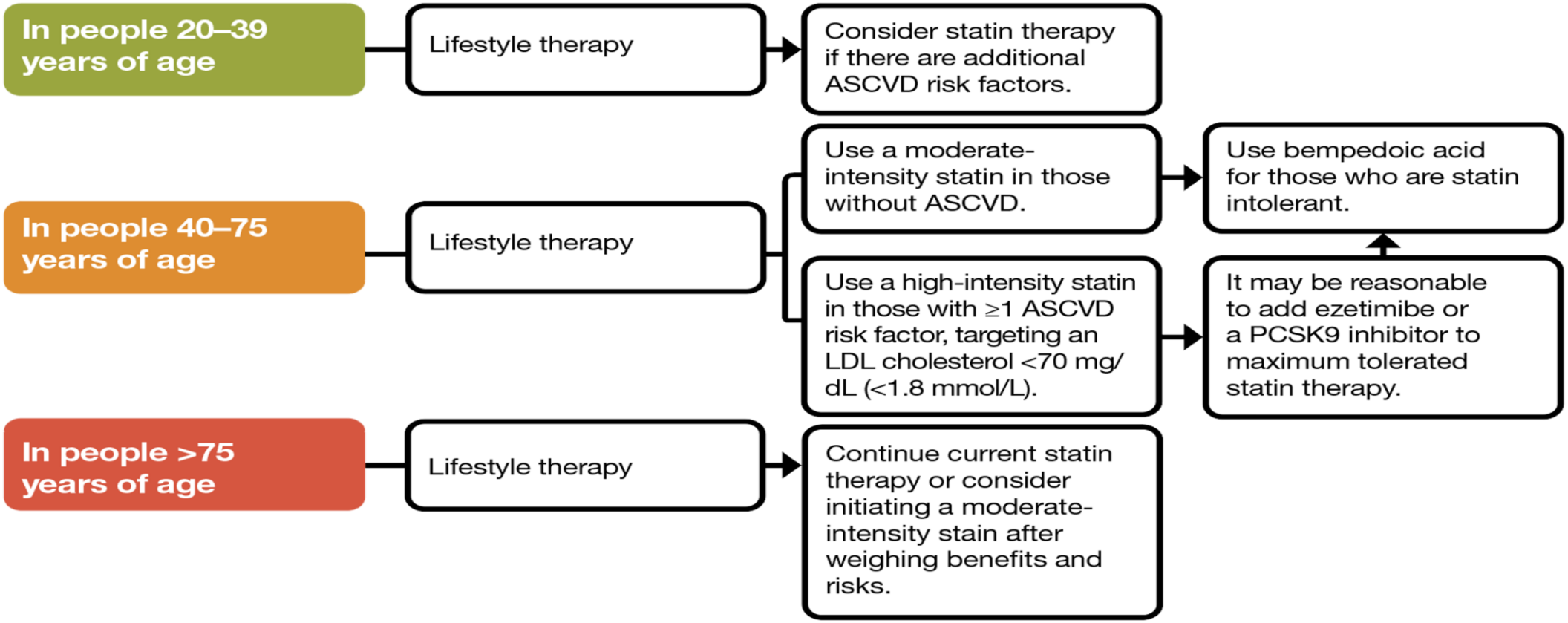
How often should you check lipids?

- For people with prediabetes or diabetes not on lipid-lowering therapy, check at diagnosis and at least annually thereafter.
- Check lipids at initiation of lipid-lowering therapy, 4–12 weeks after initiation or dose changes, and annually thereafter.

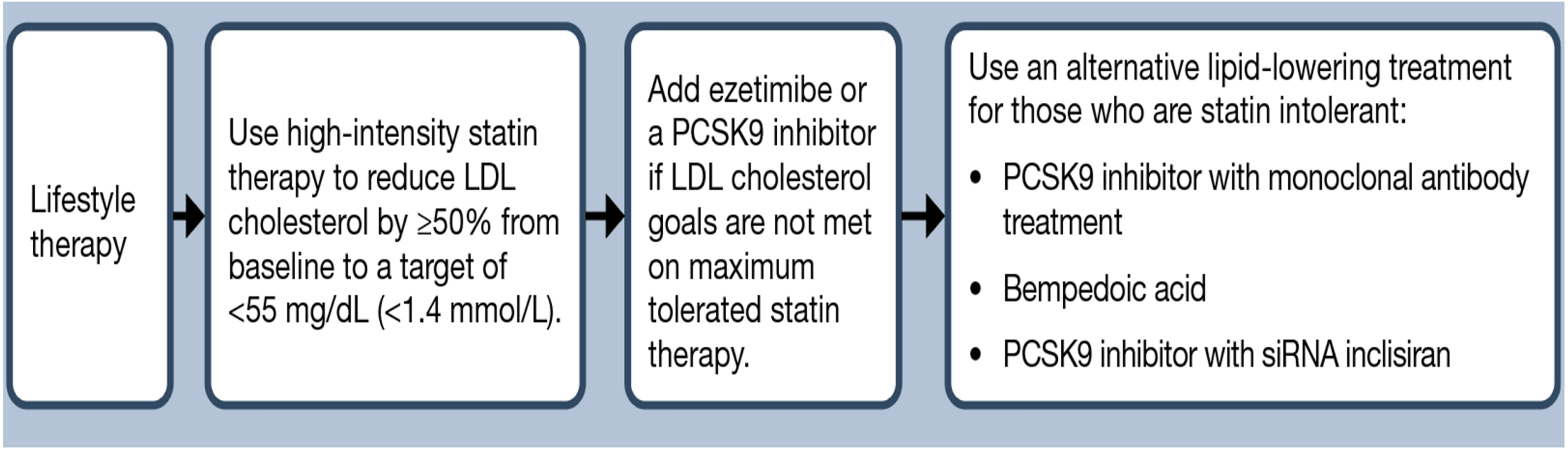
Statin Therapy Potency Chart

High-intensity statin therapy (lowers LDL cholesterol by ≥50%)	Moderate-intensity statin therapy (lowers LDL cholesterol by 30-49%)
Atorvastatin (40–80 mg) Rosuvastatin (20–40 mg)	Atorvastatin (10–20 mg) Rosuvastatin (5–10 mg) Simvastatin (20–0 mg) Pravastatin (40–80 mg) Lovastatin (40 mg) Fluvastatin XL (80 mg) Pitavastatin (1–4 mg)
Once-daily dosing. XL, extended release.	

Lipid Management for Primary Prevention of Atherosclerotic Cardiovascular Disease (ASCVD) Events in People with Diabetes



Lipid Management for Secondary Prevention of ASCVD Events in People With Diabetes of All Ages


Lifestyle therapy
Use high-intensity statin therapy to reduce LDL cholesterol by ≥50% from baseline to a target of <55 mg/dL (<1.4 mmol/L).
Add ezetimibe or a PCSK9 inhibitor if LDL cholesterol goals are not met on maximum tolerated statin therapy.
Use an alternative lipid-lowering treatment for those who are statin intolerant:
• PCSK9 inhibitor with monoclonal antibody treatment
• Bempedoic acid
• PCSK9 inhibitor with siRNA inclisiran

PCSK9, proprotein convertase subtilisin/kexin type 9.

Screening for Chronic Kidney Disease (CKD)

Who?

- **Everyone with type 2 diabetes**
- **Everyone with type 1 diabetes for ≥5 years**

How?

- **Urinary albumin-to-creatinine ratio (UACR)**
- **Estimated glomerular filtration rate (eGFR)**

How often?

- **Annually**

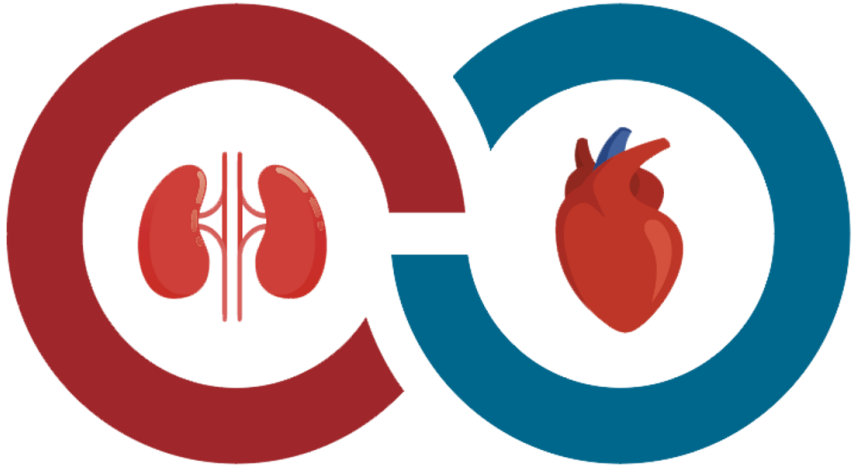
Monitoring Established CKD

How? UACR and eGFR. Use the CKD Epidemiology Collaboration's CKD-EPI Refit equation, which eliminates race as a variable, for all individuals.

How often? One to four times per year, depending on the stage of the disease

Why Manage CKD?

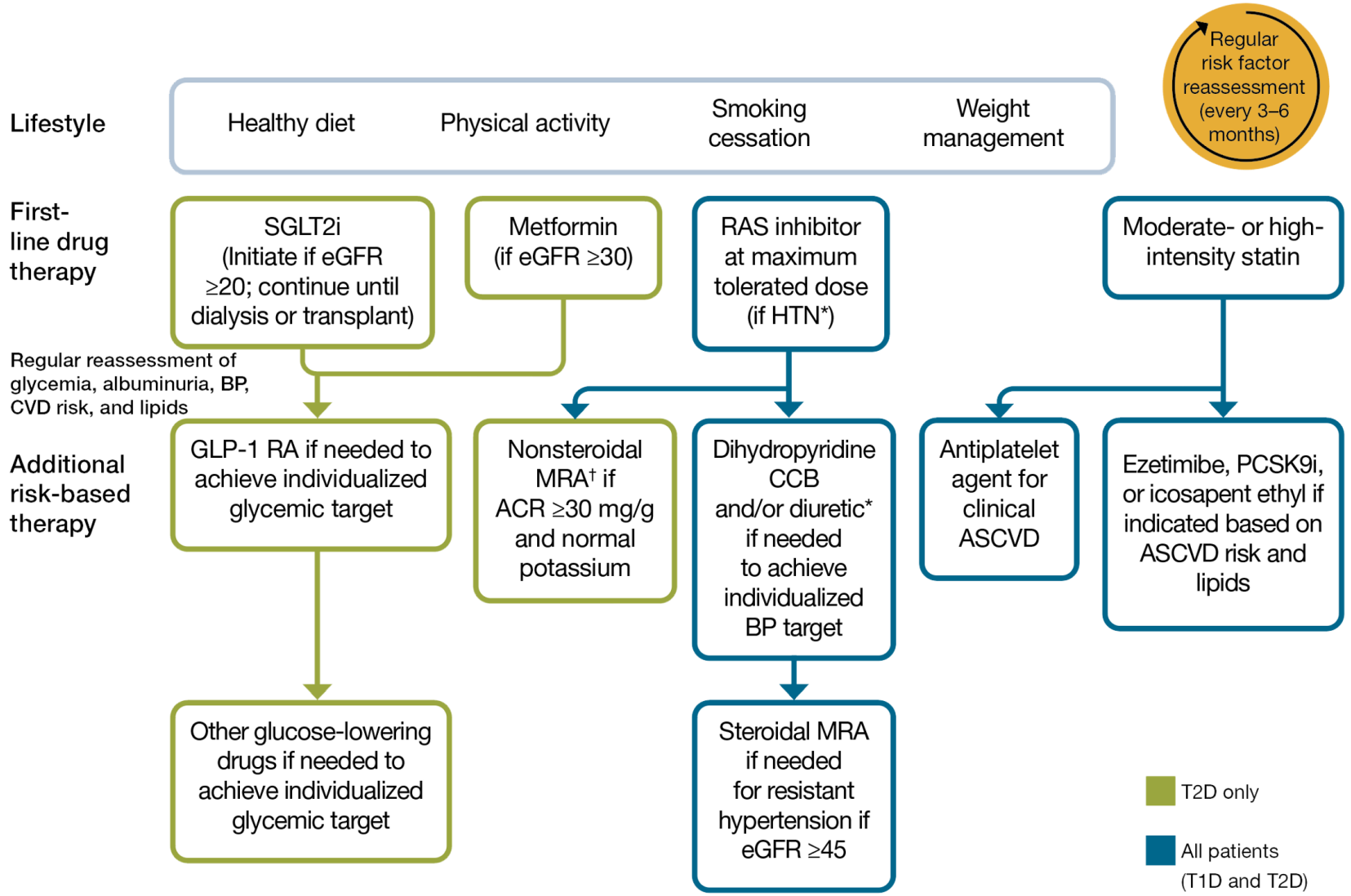
Decreases risk of CKD progression



Reduces cardiovascular risk

Kidney Disease and Risk Management

Holistic Approach to Improving Outcomes in People With Diabetes and CKD


Regular risk factor reassessment (every 3–6 months)
Lifestyle
Healthy diet
Physical activity
Smoking cessation
Weight management
First-line drug therapy
SGLT2i (Initiate if eGFR ≥20; continue until dialysis or transplant)
Metformin (if eGFR ≥30)
RAS inhibitor at maximum tolerated dose (if HTN*)
Moderate- or high-intensity statin
Regular reassessment of glycemia, albuminuria, BP, CVD risk, and lipids
Additional risk-based therapy
GLP-1 RA if needed to achieve individualized glycemic target
Nonsteroidal MRA† if ACR ≥30 mg/g and normal potassium
Dihydropyridine CCB and/or diuretic* if needed to achieve individualized BP target
Antiplatelet agent for clinical ASCVD
Ezetimibe, PCSK9i, or icosapent ethyl if indicated based on ASCVD risk and lipids
Other glucose-lowering drugs if needed to achieve individualized glycemic target
Steroidal MRA if needed for resistant hypertension if eGFR ≥45
T2D only
All patients (T1D and T2D)

Clinical Tips

- ✓ Periodically check serum creatinine and potassium levels when ACE inhibitor, angiotensin receptor blocker (ARB), or nonsteroidal mineralocorticoid receptor antagonist is used.
- ✓ Do not discontinue ACE inhibitor or ARB therapy for increases ≤30% increases in serum creatinine in the absence of volume depletion.
- ✓ Aim for a urinary albumin reduction ≥30% in people with CKD and urinary albumin ≥300 mg/g to slow CKD progression.

Section 9

Management of Diabetes in Pregnancy

By: Dr. Rezg Yousef Al-Sunah
Bachelor of Clinical Pharmacy- Pharm-D

Preconception Counseling:

- Incorporate preconception counseling into diabetes care starting at puberty and continuing in all people with diabetes and childbearing potential.
- Discuss family planning and prescribe effective contraception to be used until A1C is optimized for pregnancy.
- Address the importance of achieving glucose levels as close to normal as is safely possible, ideally A1C <6.5% (<48 mmol/mol) to reduce the risk of congenital anomalies, preeclampsia, macrosomia, preterm birth, and other complications.
- Focus on nutrition, diabetes education, and screening for diabetes comorbidities and complications, in addition to achieving glycemic targets.
- Counsel on the risk of development and/or progression of diabetic retinopathy. A dilated eye examination should occur before pregnancy or in the first trimester, with continued monitoring every trimester and for 1 year postpartum based on findings.

Glycemic Management and Goals in Pregnancy

- Perform fasting, preprandial, and postprandial blood glucose monitoring (BGM).
- Glucose goals are fasting plasma glucose <95 mg/dL (<5.3 mmol/L) and either 1-h postprandial glucose <140 mg/dL (<7.8 mmol/L) or 2-h postprandial glucose <120 mg/dL (<6.7 mmol/L).
- Ideally, the A1C goal in pregnancy is <6% (<42 mmol/mol) if this can be achieved without significant hypoglycemia; the goal may be relaxed to <7% (<53 mmol/mol) to prevent hypoglycemia.
- When used in addition to pre- and postprandial BGM, continuous glucose monitoring can help to achieve the A1C goal in diabetes and pregnancy.

Management of Gestational Diabetes Mellitus (GDM)

GDM refers specifically to diabetes diagnosed after the first trimester of pregnancy in individuals who did not have diabetes before pregnancy. Diabetes detected before or in early pregnancy is usually considered to be preexisting type 2 diabetes.

- Individuals without diabetes before or early in pregnancy should be screened for GDM at 24 to 28 weeks of pregnancy.
- Lifestyle behavior change is an essential component of GDM management.
- Insulin is the preferred medication for treating hyperglycemia in GDM.
- Metformin and glyburide should not be used as first-line agents in GDM. Other oral and noninsulin injectable glucose-lowering medications lack long-term safety data for use in GDM.

Additional Drug Considerations During Pregnancy

- Initiate or titrate blood pressure medication at a threshold of 140/90 mmHg. A target of 110–135/84 mmHg is suggested. Therapy should be reduced if blood pressure is <90/60 mmHg.
- Stop potentially harmful medications in pregnancy (i.e., ACE inhibitors, angiotensin receptor blockers, and statins) prior to conception and avoid in sexually active individuals of childbearing potential who are not using reliable contraception.

Postpartum Care

Postpartum care should include psychosocial assessment and support for self-care.

Contraception

Discuss and implement a contraception plan with all individuals with diabetes of childbearing potential.

Postpartum Care of Individuals With GDM

- Screen for diabetes at 4–12 weeks postpartum with a 75-g oral glucose tolerance test using nonpregnancy criteria.
- Lifelong diabetes screening should occur every 1–3 years.
- For those with overweight/obesity and prediabetes, implement intensive lifestyle interventions and/or metformin therapy.

Lactation

Promote breastfeeding, which has been shown to reduce the risk of type 2 diabetes later in life.

Postpartum Care for Individuals With Preexisting Diabetes

Insulin resistance decreases dramatically immediately after delivery. Evaluate insulin requirements, adjust doses, and monitor for hypoglycemia.

Thanks for your time and attention

Contact us for questions and more information

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